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NEWS	6	FEB	16	New FASTA Display Formats Added to USGENE and PCTGEN
NEWS	7	FEB	16	INPADOCDB and INPAFAMDB Enriched with New Content and Features
NEWS	8	FEB	16	INSPEC Adding Its Own IPC codes and Author's E-mail Addresses
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NEWS	14	APR	07	CA/CAplus CLASS Display Streamlined with Removal of Pre-IPC 8 Data Fields
NEWS	15	APR	07	50,000 World Traditional Medicine (WTM) Patents Now Available in CAplus
NEWS	16	APR	07	MEDLINE Coverage Is Extended Back to 1947
NEWS	17	JUN	16	WPI First View (File WPIFV) will no longer be available after July 30, 2010
NEWS		JUN	18	DWPI: New coverage - French Granted Patents
NEWS	19	JUN	18	CAS and FIZ Karlsruhe announce plans for a new STN platform
NEWS	20	JUN	18	IPC codes have been added to the INSPEC backfile (1969-2009)
NEWS	21	JUN	21	Removal of Pre-IPC 8 data fields streamline displays in CA/CAplus, CASREACT, and MARPAT
NEWS		JUN		Access an additional 1.8 million records exclusively enhanced with 1.9 million CAS Registry Numbers EMBASE Classic on STN
NEWS	23	JUN	28	Introducing "CAS Chemistry Research Report": 40 Years of Biofuel Research Reveal China Now Atop U.S. in Patenting and Commercialization of Bioethanol

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=> s Sayers J?/AU L1 385 SAYERS J?/AU

=> s 11 and growth(w)hormone

L2 22 L1 AND GROWTH(W) HORMONE

=> dup rem 12

PROCESSING COMPLETED FOR L2 L3 19 DUP REM L2 (3 DUPLICATES REMOVED)

=> s ARTYMIUK P?/AU

363 ARTYMIUK P?/AU L4

=> s 14 and growth(w)hormone

19 L4 AND GROWTH(W) HORMONE L5

=> dup rem 15

PROCESSING COMPLETED FOR L5 L6 16 DUP REM L5 (3 DUPLICATES REMOVED)

=> s ROSS R?/AU

11282 ROSS R?/AU

=> s 17 and growth(w)hormone

365 L7 AND GROWTH(W) HORMONE

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=> s 18 and ligand
L9 28 L8 AND LIGAND
=> dup rem 19
PROCESSING COMPLETED FOR L9
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              16 DUP REM L9 (12 DUPLICATES REMOVED)
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             385 S SAYERS J?/AU
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               19 DUP REM L2 (3 DUPLICATES REMOVED)
L4
             363 S ARTYMIUK P?/AU
L5
               19 S L4 AND GROWTH (W) HORMONE
L6
               16 DUP REM L5 (3 DUPLICATES REMOVED)
           11282 S ROSS R?/AU
L8
             365 S L7 AND GROWTH(W) HORMONE
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               28 S L8 AND LIGAND
               16 DUP REM L9 (12 DUPLICATES REMOVED)
L10
=> dis ibib abs 13 1-19
    ANSWER 1 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2010:238593 CAPLUS
DOCUMENT NUMBER:
                            152:304118
TITLE:
                            Glucagon-like peptide I (GLP-1) fusions with
                            GLP-1-binding proteins, such as dipeptidyl peptidase
                            IV (DDP4), and antidiabetic uses thereof
INVENTOR(S):
                           Artymiuk, Peter; Ross, Richard; Sayers, Jon
PATENT ASSIGNEE(S):
                           Asterion Ltd., UK
SOURCE:
                            PCT Int. Appl., 72pp.
                            CODEN: PIXXD2
DOCUMENT TYPE:
                            Pat.ent.
LANGUAGE:
                            English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
     PATENT NO. KIND DATE APPLICATION NO. DATE
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      WO 2010020767 A2 20100225 WO 2009-GB2006 20090818
          W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,
               CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG,
               ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP,
               KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA,
               MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE,
          PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BB, BG, CH, CY, CZ, DB, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI,
               SK, SM, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NR, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG,
               ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
                                                  GB 2008-15248 A 20080821
US 2008-90813P P 20080821
GB 2009-7794 A 20090507
GB 2009-13901 A 20090810
PRIORITY APPLN. INFO.:
```

OTHER SOURCE(S): MARPAT 152:304118

AB The inventors describe nucleic acid mols. that encode fusion polypeptides comprising GLP-1 (glucagon-like peptide I), or a receptor binding part thereof, linked directly or indirectly to a polypeptide that naturally binds GiP-1. In one embodiment GLP-1 is linked to an extracellular domain of a glucagon-like peptide-1 receptor (GLP-1 receptor, GLPR), Alternative embodiments include the fusion of GLP-1 to inactivated dipeptidyl peptidase IV (DDP4, CD26) and optionally inactive adenosine deaminase (ADA), such as in the provided GLP1/DPP4/ADA fusion protein 10G1.

L3 ANSWER 2 OF 19 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on STN

ACCESSION NUMBER: 2009:333182 BIOSIS

DOCUMENT NUMBER: PREV200900334285

TITLE: Modified growth hormone fusion

polypeptides.

AUTHOR(S): Ross, Richard [Inventor]; Anonymous; Sayers, Jon

[Inventor]; Artymiuk, Peter [Inventor]

CORPORATE SOURCE: Sheffield, United Kingdom

ASSIGNEE: Asterion Limited PATENT INFORMATION: US 07524649 20090428

SOURCE: Official Gazette of the United States Patent and Trademark

Office Patents, (APR 28 2009) CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent

LANGUAGE: English
ENTRY DATE: Entered STN: 27 May 2009

Last Updated on STN: 27 May 2009

AB The invention relates to chimeric polypeptides wherein said polypeptides

comprise a modified binding domain of growth hormone linked to a receptor binding domain of growth hormone receptor; and tandems/oligomers of said modified growth

hormone binding domains.

L3 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:1048978 CAPLUS

DOCUMENT NUMBER: 151:307229

TITLE: Linker peptides including glycosylation sites for use

in fusion proteins

INVENTOR(S): Artymiuk, Peter; Ross, Richard; Sayers, Jon

PATENT ASSIGNEE(S): Asterion Limited, UK SOURCE: PCT Int. Appl., 185pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 1

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	FI,	GB,	GD,	GE,	GH,	GM,	GT,	HN,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,
FI, GB, GD KG, KM, KN			KN,	KP,	KR,	KZ,	LA,	LC,	LK,	LR,	LS,	LT,	LU,	LY,	MA,	MD,
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	PL,	PT,	RO,	RS,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SM,	ST,	SV,	SY,	TJ,
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RW:	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	HR,	HU,
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IE, IS, IT SK, TR, BF		BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	
	TD,	TG,	BW,	GH,	GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,

ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

A 20080219 PRIORITY APPLN. INFO.: GB 2008-2978

GB 2008-21076 A 20081119 GB 2009-539 A 20090114

OTHER SOURCE(S): MARPAT 151:307229

AB Peptide linkers that contain a glycosylation site and that can be used in the manufacture of fusion proteins that interact with membranes, e.g. fusion proteins of proteins and their cognate receptors. Glycosylation site

motif variants for use in linker peptides are described.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD, ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:791326 CAPLUS

DOCUMENT NUMBER: 151:132011

TITLE: Peptide fusion proteins for cancer therapy INVENTOR(S):

Artymiuk, Peter; Ross, Richard; Sayers, Jon Asterion Limited, UK PCT Int. Appl., 36pp. PATENT ASSIGNEE(S):

SOURCE: CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

> KIND DATE APPLICATION NO. PATENT NO. KIND DATE DATE WO 2009081170 A2 20090702 A3 20091203 WO 2008-GB4279 20081224 WO 2009081170 W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,

AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA PRIORITY APPLN. INFO.: GB 2007-25201 A 20071224 We disclose fusion proteins comprising a peptide comprising a binding domain for a receptor which is linked to a polypeptide comprising the

binding domain to which said peptide binds. L3 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:457596 CAPLUS

DOCUMENT NUMBER: 150:391157

TITLE: Protein and nucleotide sequences of modified

growth hormone polypeptides Artymiuk, Peter; Ross, Richard A.; Sayers, Jon Asterion Limited, UK PCT Int. Appl., 44pp. INVENTOR(S):

PATENT ASSIGNEE(S): SOURCE:

CODEN: PIXXD2 DOCUMENT TYPE: Pat.ent.

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

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WO 2009047474 A2 20090416 WO 2008-GB3056 20080910
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              PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ,
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              AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
     AU 200839386 A1 20090416 AU 2008-309386 20088910 

KR 2010067686 A 20100621 KR 2010-710215 20080910 

KITY APPLN. INFO.: GB 2007-19910P P 20071011 

GB 2007-19818 A 20071011 

WO 2008-GB3056 W 20089050
PRIORITY APPLN. INFO.:
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The invention relates to modified growth hormone fusion proteins and dimers comprising said fusion proteins; nucleic acid mols, encoding said proteins and methods of treatment that use said proteins in the treatment of conditions that result from growth hormone excess. The protein and nucleotide sequences of modified growth hormone fusion protein for treatment of growth hormone related diseases.

L3 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:177456 CAPLUS

DOCUMENT NUMBER: 150:206809

TITLE: Insulin-like growth factor fusion proteins and

therapeutic uses thereof

INVENTOR(S): Artymiuk, Peter; Ross, Richard; Sayers, Jon PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 47pp.

CODEN: PIXXD2 Patent.

DOCUMENT TYPE: LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

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TN	SK, TR, AL, BA, MK, RS N 2010KN00777 A 2010						0521		IN 2	010-	KN77	7		2	0100	301	

GB 2007-15213 A 20070806 US 2007-956333P P 20070816 WO 2008-GB2655 W 20080805

AB This disclosure relates to insulin-like growth factor fusion polypeptides and nucleic acid mols. encoding said polypeptides. The fusion polypeptide comprises insulin-like growth factor, or active part thereof linked, directly or indirectly, to at least one insulin-like growth factor factor. The invention also deain of the insulin-like growth factor receptor. The invention also relates to methods of treating insulin-like growth factor deficiency related disorders with said polypeptides and nucleic acid mols. A method for preparing a hybridoma cell-line producing monoclonal antibodies which bind said polypeptides is also presented.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:115655 CAPLUS

DOCUMENT NUMBER: 150:161106

TITLE: Growth hormone fusion proteins

INVENTOR(S): Ross, Richard; Artymiuk, Peter; Sayers, Jon

PATENT ASSIGNEE(S): Asterion Limited, ÜK
SOURCE: PCT Int. Appl., 41pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

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			AM,	AZ,	BY,	KG,	KZ,	MD,	RU,	TJ,	TM							
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	EP	2170	943			A1		2010	0407		EP 2	008-	7759	45		2	0080	716
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												008-0			1	ii 2	0800	716

AB We disclose growth hormone fusion proteins that have increased in vivo stability and activity; nucleic acid mols. encoding said proteins and methods of treatment of growth hormone deficiency that use said proteins. This disclosure relates to the biol. actions of a ligand-receptor fusion (LR-fusion) of GH with its extracellular domain receptor. Such a genetically engineered LR-fusion protein was purified from mammalian cell culture. In rats the LR-fusion

had a 300-times reduced clearance compared to native GH and single administration promoted growth for 10 days far superior to that seen with native GH. The reduced clearance is reproducible in a primate model. The LR-fusion forms a reciprocal, head-to-tail dimer that provides a reservoir of inactive hormone as occurs naturally with GH and its binding protein. A recombinant gene encoding human GH linked to the A & B domains of the GHR extracellular domain (exCHR1-238) via a flexible (Gly4Ser)4 linker, was generated (Fig. 1 c).

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 19 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on STN

ACCESSION NUMBER: 2009:137246 BIOSIS DOCUMENT NUMBER: PREV200900137246

TITLE: Fusion protein comprising growth hormone

and growth hormone receptor.

AUTHOR(S): Ross, Richard [Inventor]; Anonymous; Artymiuk, Peter

[Inventor]; Sayers, Jon [Inventor]

CORPORATE SOURCE: Sheffield, United Kingdom ASSIGNEE: Asterion Limited

PATENT INFORMATION: US 07446183 20081104

SOURCE: Official Gazette of the United States Patent and Trademark

Office Patents, (NOV 4 2008)
CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent

LANGUAGE: English

ENTRY DATE: Entered STN: 18 Feb 2009

Last Updated on STN: 18 Feb 2009

AB This invention relates to agents which bind to cell surface receptors; methods to manufacture said agents; therapeutic compositions comprising

said agents; and screening methods to identify novel agents.

L3 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2008:352889 CAPLUS

DOCUMENT NUMBER: 148:347917
TITLE: Growth factor chimeric protein for use in non-human

animals

INVENTOR(S): Ross, Richard; Artymiuk, Peter; Sayers, Jon

PATENT ASSIGNEE(S): Asterion Limited, UK

SOURCE: PCT Int. Appl., 36pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PAT	ENT :	NO.			KIN	D	DATE			APPL	ICAT	ION :	NO.		D.	ATE	
						_											
WO	2008	0320	59		A2		2008	0320		WO 2	007-0	GB34	53		2	0070	913
WO	2008	0320	59		A3		2008	0508									
	₩:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BH,	BR,	BW,	BY,	BZ,	CA,
		CH,	CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DO,	DZ,	EC,	EE,	EG,	ES,	FI,
		GB,	GD,	GE,	GH,	GM,	GT,	HN,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,
	GB, GD, GE KM, KN, KE			KP,	KR,	KZ,	LA,	LC,	LK,	LR,	LS,	LT,	LU,	LY,	MA,	MD,	ME,
		MG,	MK,	MN,	MW,	MX,	MY,	MZ,	NA,	NG,	NI,	NO,	NZ,	OM,	PG,	PH,	PL,
		PT,	RO,	RS,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SM,	SV,	SY,	TJ,	TM,	TN,
		TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	ZA,	ZM,	ZW				
	RW:	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	HU,	IE,
		IS,	IT,	LT,	LU,	LV,	MC,	MT,	NL,	PL,	PT,	RO,	SE,	SI,	SK,	TR,	BF,
		ΒJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG,	BW,
		GH,	GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,

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BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
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US 20090270325 A1 20091029 US 2009-441361 20090319 PRIORITY APPLN. INFO.: GB 2006-18082 A 20060914 WO 2007-GB3453 W 20070913

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT AB We describe a chimeric protein comprising a growth

hormone polypeptide linked to a polypeptide comprising the extracellular binding domain of growth hormone

receptor; its use in enhancing the growth and metabolism of non-human animals and homodimers comprising said chimeric protein.

ANSWER 10 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2007:1303035 CAPLUS

DOCUMENT NUMBER: 147:535195

TITLE:

Fusion protein composed of circularly permuted

growth hormone antagonist GHCP07C, extracellular domain of receptor, and human modified

prolactin, and its use in construction of

pharmaceutical compositions for treating disorders INVENTOR(S): Pradhananga, Sarbendra; Sayers, John; Ross,

Richard; Artymiuk, Peter

English

PATENT ASSIGNEE(S): Asterion Limited, UK PCT Int. Appl., 46pp. SOURCE:

CODEN: PIXXD2 DOCUMENT TYPE: Pat.ent. LANGUAGE:

FAMILY ACC. NUM. COUNT: 1

E		ENT I				KIN	D	DATE				LICAT				D	ATE	
Ţ-						A1		2007	1115			2007-				2	0070	405
												, BG,						
			CH,	CN.	co.	CR.	CU,	CZ.	DE.	DK.	DM	, DZ,	EC.	EE.	EG.	ES,	FI,	GB,
												, IL,						
												, LT,						
			MN,	MW,	MX,	MY,	MZ,	NA,	NG,	NI,	NO	, NZ,	OM,	PG,	PH,	PL,	PT,	RO,
			RS,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SM	, SV,	SY,	TJ,	TM,	TN,	TR,	TT,
			TZ,	UA,	UG,	US,	UZ,	VC,	VN,	ZA,	ZM	, ZW						
		RW:	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE	, ES,	FI,	FR,	GB,	GR,	HU,	ΙE,
			IS,	IT,	LT,	LU,	LV,	MC,	MT,	NL,	PL	, PT,	RO,	SE,	SI,	SK,	TR,	BF,
			ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW	, ML,	MR,	NE,	SN,	TD,	TG,	BW,
			GH,	GM,	ΚE,	LS,	MW,	MZ,	NA,	SD,	SL	, SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,
								ΤJ,										
												2007-						
												2007-						
E	ΞP											2007-						
		R:										, ES,						
												, PL,						
-	JP	2009	5320.	51		T		2009	0910		JP	2009-	5036	58		2	0070	405
C	CN	1013	8964	9		A		2009	0318		CN	2007-	8000	6944		2	0080	827
												2008-						
		2008						2008				2008-						
												2008-						
	US 20100035804 ORITY APPLN. INFO.:							2010	0211									
PRIORI	LTY	APP.	LN.	TMEO	. :							2006-					0060 0070	
											WU	2007-		85				405

AB The invention provides nucleic acid mols. encoding the circularly permuted human growth hormone GHCP07 and variants thereof, wherein variants contain amino acid changes at the receptor binding sites and acts as growth hormone receptor antagonists. The

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invention also provides the amino acid sequences of GHCP07, and antagonist
     GHCP07C, wherein GHCP07C contains a C-terminal region of human
     growth hormone (GH) linked to a N-terminal region of GH,
     with a changes in amino acids at receptor binding sites, such as Glycine
     to Arginine at position 176. The invention further provides various
     fusion proteins comprised of: (a) at least two GHCP07C polypeptides linked
     in tandem; (b) extracellular binding domains of growth
     hormone receptor (GHR) linked to at least two GHCP07 polypeptides;
     (c) GHCP07C polypeptides linked to a human prolactin modified polypeptide
     (such as G129R PRL); and/or (d) GHCP07C-human modified prolactin fusions
     containing an extracellular domain of receptors, such as cytokine, GH,
     prolactin receptors. The invention was based on the general knowledge
     that the G129R mutation in PRL and G120R mutation in GH disrupt the
     structural integrity of the two receptor sites, and results in proteins
     acting as receptor antagonists. Still further, the invention provides:
     (a) nucleic acid mols. encoding the disclosed fusion proteins and their
    use in construction of vectors for recombinant protein production; and (b) the
     amino acid sequences of said extracellilar domains found in human GHR and
     the modified human prolactin (G129R). Finally, the invention provides for
     the use of the disclosed antagonists, and/or their fusion proteins, and/or
     their nucleic acids in construction of a pharmaceutical compn which can be
     use to treat various conditions, such as gigantism, acromegaly, cancer,
     diabetic retinopathy, diabetic nephropathy and/or other complications of
     diabetes and/or GH excess. In the examples, the invention presented mol.
     genetics methods used to generate circularly permutated growth
     hormone antagonists GHCP07BHis and GHCP07C, and showed that both
     proteins had antagonistic activity.
OS.CITING REF COUNT:
                              THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
                        1
                               (1 CITINGS)
REFERENCE COUNT:
                        6
                               THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
                              RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
    ANSWER 11 OF 19
                        MEDLINE on STN
                                                        DUPLICATE 1
ACCESSION NUMBER: 2007527470
                                  MEDLINE
DOCUMENT NUMBER:
                   PubMed ID: 17721547
TITLE:
                   A ligand-receptor fusion of growth
                   hormone forms a dimer and is a potent long-acting
                    agonist.
AUTHOR:
                    Wilkinson Ian R; Ferrandis Eric; Artymiuk Peter J; Teillot
                   Marc; Soulard Chantal; Touvay Caroline; Pradhananga
                   Sarbendra L; Justice Sue; Wu Zida; Leung Kin C; Strasburger
                   Christian J: Savers Jon R: Ross Richard J
CORPORATE SOURCE:
                   School of Medicine and Biomedical Sciences, Royal
                   Hallamshire Hospital, University of Sheffield, Sheffield
                   S10 2JF, UK.
                   Nature medicine, (2007 Sep) Vol. 13, No. 9, pp. 1108-13.
SOURCE:
                   Electronic Publication: 2007-08-26.
                   Journal code: 9502015, ISSN: 1078-8956, L-ISSN: 1078-8956.
PUB. COUNTRY:
                   United States
DOCUMENT TYPE:
                   Journal; Article; (JOURNAL ARTICLE)
                   (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:
                   English
FILE SEGMENT:
                   Priority Journals
ENTRY MONTH:
                   200803
ENTRY DATE:
                   Entered STN: 11 Sep 2007
                   Last Updated on STN: 13 Mar 2008
                   Entered Medline: 12 Mar 2008
    Cytokine hormones have a short plasma half-life and require frequent
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administration. For example, growth hormone replacement involves daily injections. In common with other cytokines, the extracellular domain of the growth hormone

AB

receptor circulates as a binding protein, which naturally prolongs the biological half-life of growth hormone. Here we have studied the biological actions of a ligand-receptor fusion of growth hormone and the extracellular domain of its receptor. The genetically engineered ligand-receptor fusion protein was purified from mammalian cell culture. In rats, the ligand-receptor fusion had a 300-times reduced clearance as compared to native growth hormone, and a single injection promoted growth for 10 d, far exceeding the growth seen after administration of native growth hormone. The ligand-receptor fusion forms a reciprocal, head-to-tail dimer that provides a reservoir of inactive hormone similar to the natural reservoir of growth hormone and its binding protein. In conclusion, a ligand-receptor fusion of cytokine to its extracellular receptor generates a potent, long-acting agonist with exceptionally slow absorption and elimination. This approach could be easily applied to other cytokines.

L3 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2006:104499 CAPLUS

DOCUMENT NUMBER: 144:219144

TITLE: Recombinant dimers of cytokine receptor-binding

domains linked by inflexible helical linkers for

modulation of cytokine signaling

INVENTOR(S): Artymiuk, Peter; Pradhananga, Sarbendra; Sayers, John; Ross, Richard

PATENT ASSIGNEE(S): Asterion Limited, UK

SOURCE: PCT Int. Appl., 69 pp.

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

	TENT :															ATE	
WO WO	2006 2006 2006	0108 0108	91 91		A2 A9		2006	0202 0427		WO 2						0050	
WO									-	-	ъ.	-	Dir	D17	20	0.7	011
	w:						AU,										
							DE,										
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							LU,										
							PG,										
			L, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US,														
		ZA,	ZM, ZW, SZ, BE, CY, FR, GR, IE, IT, MC, NL,								NL,	SI,	BF,	ВJ,	CF,		
		CG,	G, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD								TD,	TG					
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		CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG,	BW,	GH,
		GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY,
		KG,	KZ,	MD,	RU,	TJ,	TM										
AU	2005	2661	84		A1		2006	0202		AU 2	005-	2661	84		2	0050	718
CA	2575	441			A1		2006	0202		CA 2	005-	2575	441		2	0050	718
EP	1771	467			A2		2007	0411		EP 2	005-	7615	93		2	0050	718
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		IS,	IT,	LI,	LT,	LU,	LV,	MC,	NL,	PL,	PT,	RO,	SE,	SI,	SK,	TR	
CN	1010	1461	6		A		2007	8080		CN 2	005-	8003	0121		2	0050	718
JP	2008	5072	92		T		2008	0313		JP 2	007-	41		2	0050	718	
NZ	5532	24			A		2009	0313 JP 2007-523141 0531 NZ 2005-553224							2	0050	718
	2391																
	2007																

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KR 2007067678 A 20070628 KR 2007-703976 KR 891509 B1 200990406 IN 2007KN00631 A 20070706 IN 2007KN631 KR 200906221 A 20090114 KR 2008-729038 US 20099021477 A1 200990930 US 20099-658526
                                                                                              20070220
                                                                                                 20070221
                                                               US 2009-658526 20090416 US 2004-591358P P 20040726 GB 2004-16687 A 20040727 GB 2005-2839 A 20040727
PRIORITY APPLN. INFO.:
                                                                WO 2005-GB2826 W 20050718
KR 2007-703976 A3 20070220
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
       We disclose therapeutic proteins comprising at least two domains capable
       peptide linker, wherein the linker optionally comprises a rigid alpha
       helical region. These proteins may act as agonists or antagonists of
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of binding to a cytokine receptor, wherein the domains are connected by a cytokine signaling. Thus, growth hormone

receptor-binding growth hormone fragments were

dimerized using a rigid or semi-rigid linker. The rigid linker comprised the motif A(EAAAK)nA, with n=1-5 preferred. These proteins were produced with transgenic E. coli. The growth hormone

activity of these proteins was equal to or greater than growth hormone itself.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD

(3 CITINGS) REFERENCE COUNT: THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2005:34776 CAPLUS

DOCUMENT NUMBER: 142:127937

TITLE: Modified cytokine ligand polypeptides preparation,

screening, and uses thereof for treatment

INVENTOR(S): Sayers, Jon; Artymuik, Peter; Ross, Richard PATENT ASSIGNEE(S): Asterion Limited, UK

SOURCE: PCT Int. Appl., 45 pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent.

LANGUAGE: English FAMILY ACC. NUM. COUNT: 1

	TENT :				KIN	D	DATE			APPL		ION 1			D.	ATE	
WO	2005 2005	0031	65					0113 0714		WO 2					2	0040	628
	W:	AE, CN, GE, LK, NO, TJ, BW, AZ,	AG, CO, GH, LR, NZ, TM, GH, BY,	AL, CR, GM, LS, OM, TN, GM, KG,	AM, CU, HR, LT, PG, TR, KE, KZ,	AT, CZ, HU, LU, PH, TT, LS, MD,	AU, DE, ID, LV, PL, TZ, MW, RU,	AZ, DK, IL, MA, PT, UA, MZ, TJ,	DM, IN, MD, RO, UG, NA, TM,	DZ, IS, MG, RU, US, SD, AT,	EC, JP, MK, SC, UZ, SL, BE,	EE, KE, MN, SD, VC, SZ, BG,	EG, KG, MW, SE, VN, TZ, CH,	ES, KP, MX, SG, YU, UG, CY,	FI, KR, MZ, SK, ZA, ZM, CZ,	GB, KZ, NA, SL, ZM, ZW, DE,	GD, LC, NI, SY, ZW AM, DK,
CA	2568	SI, SN,	SK, TD,	TR,	BF,	BJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,		NE,
							0329		EP 2	004-	7431	75		2	0040	628	
LIL		AT,	BE,	CH,	DE,	DK,	ES,	FR, BG,	GB,					NL,	SE,	MC,	PT,

JP 2008504001 AT 466880 US 20070264234 PRIORITY APPLN, INFO.:	T T A1	20080214 20100515 20071115	AT US	2006-518330 2004-743175 2007-561831 2003-15182	A	20040628 20040628 20070316 20030628
PRIORITI APPLN. INFO.:				2003-13182 2004-GB2827		20030628

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The disclosed invention describes modified cytokine ligand polypeptides comprising a modified amino acid sequence which is a modification of the native cytokine amino acid sequence of said ligand, wherein the native N terminal am C terminal amino acid residues of the native polypeptide are linked, directly or indirectly, together, characterized in that said ligand is provided with alternative N terminal and C terminal amino acid residues and further wherein at least one binding domain for said ligand's cognate binding partner or receptor complex is disrupted. The authors describe the first embodient of the growth hormone circular permutation GH CPO1, with the N terminus Ile121 and the C terminus Glul18. The "old" termini GH were linked by a 6 amino acid linker, formed by joining the "old" termini-3 amino acids from the first helix at the N terminus and +3 residues for the last helix at the C terminus. E. coli cells were used as the expression system. Also

terminus. E. coli cells were used as the expression system. Also described are alternative approaches to construct circular permutations of GH. OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD

(2 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:878488 CAPLUS

DOCUMENT NUMBER: 141:344597

TITLE: Chimeric proteins containing cytokine receptor binding

domain and glycosylphosphatidylinositol anchor and

their therapeutic uses
INVENTOR(S): Ross, Richard; Sayers, Jon; Artymiuk, Peter

PATENT ASSIGNEE(S): Asterion Limited, UK

SOURCE: PCT Int. Appl., 40 pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

	TENT				KIN		DATE			APPL						ATE		
WO	2004	0901	35		A2		2004	1021		WO 2						0040		
		AE, CN, GE, LK,	AG, CO, GH, LR,	AL, CR, GM, LS,	AM, CU, HR, LT,	AT, CZ, HU, LU,	AU, DE, ID, LV,	AZ, DK, IL, MA,	DM, IN, MD,	DZ, IS, MG,	EC, JP, MK,	EE, KE, MN,	EG, KG, MW,	ES, KP, MX,	FI, KR, MZ,	GB, KZ, NA,	GD, LC, NI,	
	LK, LR, L NO, NZ, O TJ, TM, TI RW: BW, GH, GI BY, KG, K ES, FI, FI SK, TR, BI			TN, GM, KZ, FR,	TR, KE, MD, GB,	TT, LS, RU, GR,	TZ, MW, TJ, HU,	UA, MZ, TM, IE,	UG, SD, AT, IT,	US, SL, BE, LU,	UZ, SZ, BG, MC,	VC, TZ, CH, NL,	VN, UG, CY, PL,	YU, ZM, CZ, PT,	ZA, ZW, DE, RO,	ZM, AM, DK, SE,	ZW AZ, EE, SI,	
EP	TD, TG 1616010 R: AT, BE, CH, IE, SI, LT,			DE,	DK,	ES,	FR,	GB ,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,		
JP	IE, SI, L 2007527695				T		2007	1004		JP 2	006-	5061	14		2	0040	407	

US 20060205926 A1 20060914 US 2005-552388 20051007 US 7625998 B2 20091201 PRIORITY APPLN. INFO.: GB 2003-8088 A 20030409 GB 2003-24235 A 20031016 WO 2004-GB1572 W 20040407 ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT The present invention relates to polypeptides which comprise a ligand-binding domain of a cytokine receptor fused with a signal sequence for the attachment of glycosylphosphatidylinositol (GPI) anchors. GPI-anchors are post-translational modifications to proteins that add

glycosylphosphatidylinositol which enable these proteins to anchor to the extracellular side of cell membranes. 1B1-GP1 was constructed, in which GH was linked through its C-terminus to the extracellular domain of the GH receptor and then linked to the GPI signal sequence. 1C1-GPI was also constructed, in which a tandem of GH was linked through the second GH C-terminus to the GPI signal sequence. The invention provides vectors and CHO-K1 cells for expressing GHBP-GPI.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD

(1 CITINGS)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 15 OF 19 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on

STN

ACCESSION NUMBER: 2004:225928 BIOSIS

DOCUMENT NUMBER:

PREV200400225966 Tandem fusions of growth hormone and

its G120R mutated antagonist retain biological activity and

demonstrate prolonged plasma half-life.

AUTHOR(S): Pradhananga, S. L. [Reprint Author]; Wilkinson, I. [Reprint Author]; Haylor, J. [Reprint Author]; Rezaee, S. [Reprint

Author]; Artymiuk, P.; Sayers, J.; Ross, R. J. M.

[Reprint Author]

CORPORATE SOURCE: Department of Clinical Sciences, Sheffield University,

Sheffield, UK

SOURCE: Growth Hormone & IGF Research, (April 2004) Vol. 14, No. 2,

pp. 116. print. Meeting Info.: Second International GH-IGF Symposium.

Queensland, Australia. April 18-22, 2004.

ISSN: 1096-6374 (ISSN print).

DOCUMENT TYPE: Conference; (Meeting)

Conference: Abstract: (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 21 Apr 2004

Last Updated on STN: 21 Apr 2004

L3 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2003:591215 CAPLUS

DOCUMENT NUMBER:

139:144956 TITLE:

Ligand binding domains of cytokine which are linked via flexible polypeptide linker and uses in therapy

INVENTOR(S): Ross, Richard; Artymiuk, Peter; Sayers, Jon

PATENT ASSIGNEE(S): Asterion Limited, UK

PCT Int. Appl., 37 pp. SOURCE: CODEN: PIXXD2

DOCUMENT TYPE: Pat.ent.

LANGUAGE: English FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

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        WO
        2003062276
        A2
        20030731
        WO
        2003-GB253
        20030124

        WO
        2003062276
        A3
        20031016

          W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
               CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
               GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
               PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
               UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
           RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
               KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
               FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
               BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2510751 A1 20030731 CA 2003-2510751 20030124
EP 1468020 A2 20041020 EP 2003-702702 20030124
          R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
               IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
JF 2005529583 T 20051006 JP 2003-562153 20030124
RU 2325400 C2 20080527 RU 2004-121969 20030124
MX 2004007160 A 20050331 MX 2004-7160 20040730
BR 2004003173 A 20060321 BR 2004-3173 20040730
US 20050214762 A1 20050929 US 2005-502344 20050512
PRIORITY APPLN. INFO:: B 20050929 W 2003-GB253 W 20030124
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
    The invention relates to the provision of oligomeric polypeptides (dimers,
      trimers, etc) comprising the ligand binding domains of cytokines which are
      linked via flexible polypeptide linker mols. The linker mols. optionally
      comprise protease sensitive sites to modulate the release of biol. active
     cytokines when administered to a human or animal subject. The invention
     also relates to chemical crosslinkers wherein the chemical crosslinkers serve
t.o
      link the ligand binding domains. The chimeric cytokine can be used for
      treating acromegaly, gigantism, GH deficiency, Turners syndrome, renal
      failure, osteoporosis, diabetes mellitus, cancer, obesity, insulin
      resistance, hyperlipidemia, hypertension, anemia, autoimmune and
      infectious disease, inflammatory disorders including rheumatoid arthritis.
OS.CITING REF COUNT: 1
                                   THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
                                    (1 CITINGS)
REFERENCE COUNT:
                                    THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
                                    RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L3 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2003:949911 CAPLUS
DOCUMENT NUMBER:
                            140:13709
TITLE:
                            Polypeptide having a plurality of modified
                             growth hormone receptor binding
                             domains from growth hormone, and
                             therapeutic use
INVENTOR(S): Ross, Richard; Sayers, Jon; Artymuik, Peter PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: Brit. UK Pat. Appl., 31 pp.
                             CODEN: BAXXDU
DOCUMENT TYPE:
                            Patent
LANGUAGE:
                             English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:
     PATENT NO. KIND DATE APPLICATION NO. DATE
GB 2389115 A 20031203 GB 2003-20479 20011214
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GB 2389115	В	20050316				
GB 2384001	A	20030716	GB	2001-30052		20011214
GB 2384001	В	20040204				
AU 2008201889	A1	20080522	AU	2008-201889		20080430
PRIORITY APPLN. INFO.:			GB	2001-30052	A3	20011214
			AU	2002-366325	A3	20021206

AB A chimeric polypeptide having a first and a second modified growth hormone receptor binding domain from growth hormone wherein the modification may be a deletion, substitution or addition of at least one amino acid residue and the said binding domains are joined in tandem. The binding domain may be modified in one of either site 1 or site 2 or at both sites 1 and 2. Specific modifications of said sites are disclosed as are linkers, polynucleotides encoding said polypeptides, vectors, cells expressing said polypeptide and methods of expressing said polypeptides. Pharmaceutical compns. comprising said polypeptides and their uses in treating diseases such as giantism, acromegaly, cancer, diabetic retinopathy, nephropathy or complications are claimed. The polypeptide may have a plurality of modified binding domains, especially those modified at site 2.

REFERENCE COUNT: THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2003:550165 CAPLUS

DOCUMENT NUMBER: 139:112729

TITLE: Chimeric growth hormone-

growth hormone receptor proteins and therapeutic uses thereof

INVENTOR(S):

Ross, Richard; Sayers, Jon; Artymuik, Peter

PATENT ASSIGNEE(S): Asterion Limited, UK

SOURCE: Brit. UK Pat. Appl., 46 pp. CODEN: BAXXDU

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PA:	PATENT NO.				KIN)	DATE			APPL	ICAT:	ION I	NO.		D	ATE	
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GB	2384	001			A		2003	0716		GB 2	001-	3005	2		2	0011	214
GB	2384	001			В		2004	0204									
GB	2389	115			A		2003	1203		GB 2	003-	2047	9		2	0011	214
GB	2389	115			В		2005	0316									
CA	2468	439			A1		2003	0828		CA 2	002-	2468	439		2	0021	206
WO	2003	0707	65		A2		2003	0828		WO 2	002-	GB55	23		2	0021	206
WO	2003	0707	65		A3		2003	1127									
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				CI, CM, GA, GN, G Al 200309						AU 2	002-	3663	25		2	0021	206
AU	2002	002366325 B2					2008	0424									
EP	1456385 A2						2004	0915		EP 2	002-	8068	58		2	0021	206
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HU	2004002496	A2	20050329	HU	2004-2496		20021206
CN	1604965	A	20050406	CN	2002-824781		20021206
CN	100558899	C	20091111				
JP	2005525106	T	20050825	JP	2003-569672		20021206
NZ	533550	A	20060224	NZ	2002-533550		20021206
NZ	543369	A	20070831	NZ	2002-543369		20021206
RU	2346047	C2	20090210	RU	2004-117777		20021206
CN	101638437	A	20100203	CN	2009-1016402	26	20021206
SG	160205	A1	20100429	SG	2007-5155		20021206
IN	2004KN00751	A	20060421	IN	2004-KN751		20040603
IN	227610	A1	20090116				
ZA	2004004488	A	20060329	ZA	2004-4488		20040607
MX	2004005675	A	20050419	MX	2004-5675		20040611
BR	2004003522	A	20060411	BR	2004-3522		20040825
US	20050123558	A1	20050609	US	2005-498497		20050114
US	7524649	B2	20090428				
ZA	2006000149	A	20061025	ZA	2006-149		20060106
KR	2006106862	A	20061012	KR	2006-716929		20060823
KR	848802	B1	20080728				
	2007108254		20071108	KR	2007-721636		20070920
	879553	B1	20090122				
	2008KN01333		20081226		2008-KN1333		20080402
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	20090239801		20090924		2009-389022		20090219
	2010043100	A	20100225		2009-223065		20090928
PRIORITY	APPLN. INFO.:				2001-30052		20011214
				AU	2002-366325		20021206
					2002-824781		20021206
					2003-569672		20021206
					2002-533550		20021206
					2002-GB5523	W	20021206
					2004-KN751		20040603
					2004-709055		20040611
					2005-498497		20050114
					2006-716929		20060823
ASSTONME	MT HISTORY FOR	HS DATEMT	AVATLABLE	TNI T	VATERIA 202	FORMAT	

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB A chimeric polypeptide comprising at least one modified binding domain of growth hormone (GH) and a ligand binding domain of

growth hormone receptor (GHR) is claimed, wherein the modification is the addition, deletion or substitution of at least one amino

acid. Said binding domain may be site 1 of growth hormone, site 2 of growth hormone or both

sites of growth hormone. The binding domain of the

growth hormone receptor may be the extracellular domain

of GHR more preferably the C-terminal SD-100 domain. Nucleic acids encoding such polypeptides, expression vectors and cells expressing such vectors are also claimed. The use of such polypeptides in the preparation of pharmaceuticals and in the treatment of diseases including gigantism,

acromegaly, cancer and diabetic conditions is also claimed. Alternatively

claimed is a chimeric polypeptide comprising more than two modified growth hormone binding domains.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2001:924005 CAPLUS

DOCUMENT NUMBER: 136:49347

TITLE: Chimeric binding agent comprising cytokine, linker and cytokine receptor and uses in modulating receptor

activity and therapy

INVENTOR(S): Ross, Richard; Artymiuk, Peter; Sayers, Jon PATENT ASSIGNEE(S): Asterion Limited, UK SOURCE: PCT Int. Appl., 79 pp.

CODEN: PIXXD2 DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

KIND DATE APPLICATION NO. DATE PATENT NO. WO 2001096565 A2 20011220 WO 2001-GB2645 20010618 WO 2001096565 A3 20020801

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

20011220 CA 2001-2447632 20010618 20030312 EP 2001-940731 20010618 CA 2447632 EP 1290170 A1 A2 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

N: AL, DE, CH, UE, UK, ES, FR, GB, GR, IT, LI, LU, NL
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2004503243 T 20040205 JP 2002-510682
US 2004007165 A1 20040415 US 2003-311473
US 7446183 B2 20081104
US 20090054336 A1 20090226 US 2008-175582
PRIORITY APPLN. INFO: GB 2000-14765 20030718

US 2008-175582 20080718 GB 2000-14765 A 20000616 GB 2001-5969 A 20010310 GB 2001-6487 A 20010316 WO 2001-GB2645 W 20010618 US 2003-311473 A1 20030718

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT AB The invention provides a binding agent comprising a first part capable of

binding a ligand binding domain of a receptor linked to a second part comprising a receptor binding domain wherein said binding agent modulates the activity of the receptor. The inventors link growth

hormone (GH), through its C-terminal and a linker to the N-terminus of the SD100 domain of growth hormone

receptor (GHR). By varying the length of the linker inventors define a mol. that has the flexibility to allow binding of GH through site 1 to full length receptor at the cell surface. The invention also relates to

methods, vectors and host cells for production of said chimeric binding agent. OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> FIL STNGUIDE SINCE FILE COST IN U.S. DOLLARS TOTAL ENTRY SESSION 84.76 FULL ESTIMATED COST 84.98 SINCE FILE TOTAL ENTRY SESSION DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) CA SUBSCRIBER PRICE -12.75-12.75

FILE 'STNGUIDE' ENTERED AT 15:01:53 ON 28 JUN 2010

USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT COPYRIGHT (C) 2010 AMERICAN CHEMICAL SOCIETY (ACS)

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jun 25, 2010 (20100625/UP).

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(FILE 'HOME' ENTERED AT 14:56:38 ON 28 JUN 2010)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 14:57:00 ON 28 JUN 2010 L1 385 S SAYERS J?/AU

L2 22 S L1 AND GROWTH(W) HORMONE

L3 19 DUP REM L2 (3 DUPLICATES REMOVED)

L4 363 S ARTYMIUK P?/AU

L5 19 S L4 AND GROWTH(W) HORMONE

L6 16 DUP REM L5 (3 DUPLICATES REMOVED) L7 11282 S ROSS R2/AU

L7 11282 S ROSS R?/AU L8 365 S L7 AND GROWTH(W)HORMONE

L9 28 S L8 AND LIGAND

L10 16 DUP REM L9 (12 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 15:01:53 ON 28 JUN 2010

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YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, BIOSIS, CAPLUS' - CONTINUE? (Y)/N:y

L6 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2010:238593 CAPLUS

DOCUMENT NUMBER: 152:304118

TITLE: Glucagon-like peptide I (GLP-1) fusions with

GLP-1-binding proteins, such as dipeptidyl peptidase

IV (DDP4), and antidiabetic uses thereof
INVENTOR(S): Artymiuk, Peter; Ross, Richard; Sayers, Jon

PATENT ASSIGNEE(S): Asterion Ltd., UK

SOURCE: PCT Int. Appl., 72pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

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	2010				A2	_	2010	0225							2	0090	818
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		MD,	ME,	MG,	MK,	MN,	MW,	MX,	MY,	ΜZ,	NA,	NG,	NI,	NO,	NZ,	OM,	PE,
		PG,	PH,	PL,	PT,	RO,	RS,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SM,	ST,	SV,
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	RW:	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FΙ,	FR,	GB,	GR,	HR,	HU,
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							GM,						SD,	SL,	SZ,	TZ,	UG,
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PRIORITY	APP	LN.	INFO	. :						GB 2	008-	1524	8	- 1	A 2	0080	821

US 2008-90813P P 20080821 GB 2009-7794 A 20090507 GB 2009-13901 A 20090810

OTHER SOURCE(S):

MARPAT 152:304118

The inventors describe nucleic acid mols. that encode fusion polypeptides comprising GLP-1 (glucagon-like peptide I), or a receptor binding part thereof, linked directly or indirectly to a polypeptide that naturally binds GLP-1. In one embodiment GLP-1 is linked to an extracellular domain of a glucagon-like peptide-1 receptor (GLP-1 receptor, GLP1R). Alternative embodiments include the fusion of GLP-1 to inactivated dipeptidyl peptidase IV (DDP4, CD26) and optionally inactive adenosine deaminase (ADA), such as in the provided GLP1/DPP4/ADA fusion protein 10G1.

ANSWER 2 OF 16 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on STN

ACCESSION NUMBER: 2009:333182 BIOSIS DOCUMENT NUMBER: PREV200900334285

TITLE: Modified growth hormone fusion

polypeptides.

AUTHOR(S): Ross, Richard [Inventor]; Anonymous; Sayers, Jon

[Inventor]; Artymiuk, Peter [Inventor]

CORPORATE SOURCE: Sheffield, United Kingdom

ASSIGNEE: Asterion Limited

PATENT INFORMATION: US 07524649 20090428

SOURCE: Official Gazette of the United States Patent and Trademark

Office Patents, (APR 28 2009) CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent

LANGUAGE: English

ENTRY DATE: Entered STN: 27 May 2009 Last Updated on STN: 27 May 2009

The invention relates to chimeric polypeptides wherein said polypeptides

comprise a modified binding domain of growth hormone linked to a receptor binding domain of growth hormone receptor; and tandems/oligomers of said modified growth

hormone binding domains.

ANSWER 3 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:1048978 CAPLUS

DOCUMENT NUMBER: 151:307229

TITLE: Linker peptides including glycosylation sites for use

in fusion proteins

INVENTOR(S): Artymiuk, Peter: Ross, Richard: Savers, Jon

PATENT ASSIGNEE(S): Asterion Limited, UK PCT Int. Appl., 185pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT 1	10.			KIN	D	DATE			APPL	ICAT	ION :	NO.		D	ATE	
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WO 2009:	10396	65		A1		2009	0827		WO 2	009-	3B43	7		2	0090	218
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						CU,										
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	ME,	MG,	MK,	MN,	MW,	MX,	MY,	MZ,	NA,	NG,	NI,	NO,	NZ,	OM,	PG,	PH,
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PRIORITY APPLN. INFO::

GB 2008-2978

GB 2008-21076

GB 2009-539

A 20081119
```

OTHER SOURCE(S): MARPAT 151:307229

B Peptide linkers that contain a glycosylation site and that can be used in the manufacture of fusion proteins that interact with membranes, e.g. fusion proteins of proteins and their cognate receptors. Glycosylation site

motif variants for use in linker peptides are described.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:791326 CAPLUS

DOCUMENT NUMBER: 151:132011

TITLE: Peptide fusion proteins for cancer therapy
INVENTOR(S): Artymiuk, Peter; Ross, Richard; Savers, Jon

PATENT ASSIGNEE(S): Asterion Limited, UK SOURCE: PCT Int. Appl., 36pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

PAT	ENT	NO.			KIN	D	DATE			APPL	ICAT	ION I	NO.		D	ATE	
	2009	0811	70		A2		2009			WO 2	008-	GB42	79		2	0081	224
WO	2009	0811	70		A3		2009	1203									
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RITY	APP	LN.	INFO	. :						GB 2	007-	2520	1		A 2	0071	224

PRIORITY APPLN. INFO.: GB 2007-25201 A 2007122
AB We disclose fusion proteins comprising a peptide comprising a binding domain for a receptor which is linked to a polypeptide comprising the binding domain to which said peptide binds.

.6 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:457596 CAPLUS DOCUMENT NUMBER: 150:391157

TITLE: Protein and nucleotide sequences of modified

growth hormone polypeptides

INVENTOR(S): Artymiuk, Peter; Ross, Richard A.; Sayers,

PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 44pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT	.00		KIN	D	DATE			APPL	ICAT	ION I	NO.		D.	ATE	
WO 2009	047474		A2		2009	0416		WO 2	008-	GB30	56		2	0080	910
W:	AE, AG,	AL,	AM,	AO,	AT,	AU,	AZ,	BA,	BB,	BG,	BH,	BR,	BW,	BY,	BZ,
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	FI, GB,	GD,	GE,	GH,	GM,	GT,	HN,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,
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RW:	AT, BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	HR,	HU,
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	TR, BF,	BJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,
	TG, BW,	GH,	GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,
	AM, AZ,	BY,	KG,	KZ,	MD,	RU,	TJ,	TM							
AU 2008	309386		A1		2009	0416		AU 2	008-	3093	86		2	0800	910
KR 2010	067686 A				2010	0621		KR 2	010-	7102	15		2	0800	910
PRIORITY APP	RIORITY APPLN. INFO.:							US 2	007-	9790	10P	1	P 2	0071	010
								GB 2	007-	1981	8	- 1	A 2	0071	011
								WO 2	008-0	GB30.	56	1	W 2	0080	910

The invention relates to modified growth hormone fusion proteins and dimers comprising said fusion proteins; nucleic acid mols. encoding said proteins and methods of treatment that use said proteins in the treatment of conditions that result from growth hormone excess. The protein and nucleotide sequences of modified growth hormone fusion protein for treatment of growth hormone related diseases.

ANSWER 6 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN ACCESSION NUMBER: 2009:177456 CAPLUS

DOCUMENT NUMBER: 150:206809

TITLE: Insulin-like growth factor fusion proteins and

therapeutic uses thereof

INVENTOR(S): Artymiuk, Peter; Ross, Richard; Sayers, Jon PATENT ASSIGNEE(S): Asterion Limited, UK

SOURCE: PCT Int. Appl., 47pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent English

LANGUAGE: FAMILY ACC. NUM. COUNT: 1

PAT	PATENT NO. WO 2009019465				KIN	D	DATE			APPL		ION I				ATE	
WO	2009	0194	65		A1		2009	0212		WO 2	008-	GB26	55		2	0080	805
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		AM,	AZ,	BY,	KG,	KZ,	MD,	RU,	TJ,	TM							

US 2007-956333P

P 20070816

WC 2008-GB2655 W 20080805

BT This disclosure relates to insulin-like growth factor fusion polypeptides and nucleic acid mols. encoding said polypeptides. The fusion polypeptide comprises insulin-like growth factor, or active part thereof linked, directly or indirectly, to at least one insulin-like growth factor-binding domain of the insulin-like growth factor receptor. The invention also relates to methods of treating insulin-like growth factor deficiency related disorders with said polypeptides and nucleic acid mols. A method for preparing a hybridoma cell-line producing monoclonal antibodies which bind said polypeptides is also presented.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:115655 CAPLUS

DOCUMENT NUMBER: 150:161106

TITLE: Growth hormone fusion proteins

INVENTOR(S): Ross, Richard; Artymiuk, Peter; Sayers, Jon

PATENT ASSIGNEE(S): Asterion Limited, UK SOURCE: PCT Int. Appl., 41pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PA'						D	DATE						NO.		D	ATE	
WO	2009	0134	61		A1		2009	0129		WO 2	008-	GB24	06		2	080	716
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		FI,	GB,	GD,	GE,	GH,	GM,	GT,	HN,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,
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AU	2008	2789	07		A1		2009	0129		AU 2	008-	2789	07		2	080	716
CA	2693	951			A1		2009	0129		CA 2	008-	2693	951		2	080	716
EP	2170	943			A1		2010	0407		EP 2	008-	7759	45		2	0800	716
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		SK,	TR,	AL,	BA,	MK,	RS										
KR	KR 2010043201 A 201					2010	0428		KR 2	010-	7021	92		2	0800	716	
CN	CN 101679504 A						2010	0324		CN 2	008-	8002	1473		2	0091	222
PRIORIT:	IORITY APPLN. INFO.:									US 2	007-	9511:	22P		A 2	0070	720
										GB 2	007-	1798	5	- 1	A 2	0070	914
										WO 2	008-	GB24	06	1	W 2	0800	716

AB We disclose growth hormone fusion proteins that have increased in vivo stability and activity; nucleic acid mols. encoding said

proteins and methods of treatment of growth hormone deficiency that use said proteins. This disclosure relates to the biol. actions of a ligand-receptor fusion (LR-fusion) of GH with its extracellular domain receptor. Such a genetically engineered LR-fusion protein was purified from mammalian cell culture. In rats the LR-fusion had a 300-times reduced clearance compared to native GH and single administration promoted growth for 10 days far superior to that seen with native GH. The reduced clearance is reproducible in a primate model. The LR-fusion forms a reciprocal, head-to-tail dimer that provides a reservoir of inactive hormone as occurs naturally with GH and its binding protein. A recombinant gene encoding human GH linked to the A & B domains of the

was generated (Fig. 1 c).
REFERENCE COUNT: 6

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 16 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on STN

GHR extracellular domain (exGHR1-238) via a flexible (Gly4Ser)4 linker,

ACCESSION NUMBER: 2009:137246 BIOSIS DOCUMENT NUMBER: PREV200900137246

TITLE: Fusion protein comprising growth hormone

and growth hormone receptor.

AUTHOR(S): Ross, Richard [Inventor]; Anonymous; Artymiuk,

Peter [Inventor]; Sayers, Jon [Inventor]

CORPORATE SOURCE: Sheffield, United Kingdom

ASSIGNEE: Asterion Limited

PATENT INFORMATION: US 07446183 20081104

SOURCE: Official Gazette of the United States Patent and Trademark

Office Patents, (NOV 4 2008)

CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent

LANGUAGE: English
ENTRY DATE: Entered STN:

ENTRY DATE: Entered STN: 18 Feb 2009 Last Updated on STN: 18 Feb 2009

AB This invention relates to agents which bind to cell surface receptors; methods to manufacture said agents; therapeutic compositions comprising

said agents; and screening methods to identify novel agents.

L6 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2008:352889 CAPLUS

DOCUMENT NUMBER: 148:347917

TITLE: Growth factor chimeric protein for use in non-human

animals

INVENTOR(S): Ross, Richard; Artymiuk, Peter; Sayers, Jon

PATENT ASSIGNEE(S): Asterion Limited, UK SOURCE: PCT Int. Appl., 36pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT NO.		KIND	DATE	APPL	ICATION :	NO.	D	ATE	
WO 200803205	9	A2	20080320	WO 2	007-GB34	53	2	00709	13
WO 200803205	9	A3	20080508						
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CH, C	CN, CO,	CR, CU,	CZ, DE,	DK, DM,	DO, DZ,	EC, E	EG,	ES,	FI,
GB,	GD, GE,	GH, GM,	GT, HN,	HR, HU,	ID, IL,	IN, IS	JP,	KE,	KG,
KM,	KN, KP,	KR, KZ,	LA, LC,	LK, LR,	LS, LT,	LU, L	, MA,	MD,	ME,
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PT, I	RO, RS,	RU, SC,	SD, SE,	SG, SK,	SL, SM,	SV, S	, TJ,	TM,	TN,

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            GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
            BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
    US 20090270325
                        A1 20091029
                                           US 2009-441361
                                                                 20090319
PRIORITY APPLN. INFO .:
                                           GB 2006-18082
                                                             A 20060914
                                           WO 2007-GB3453
                                                             W 20070913
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ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT AB We describe a chimeric protein comprising a growth

hormone polypeptide linked to a polypeptide comprising the

extracellular binding domain of growth hormone

receptor; its use in enhancing the growth and metabolism of non-human animals and homodimers comprising said chimeric protein.

L6 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN 2007:1303035 CAPLUS

ACCESSION NUMBER:

DOCUMENT NUMBER: 147:535195

TITLE: Fusion protein composed of circularly permuted

growth hormone antagonist GHCP07C,

extracellular domain of receptor, and human modified

prolactin, and its use in construction of

pharmaceutical compositions for treating disorders Pradhananga, Sarbendra; Sayers, John; Ross, Richard;

INVENTOR(S): Artymiuk, Peter

PATENT ASSIGNEE(S): Asterion Limited, UK SOURCE: PCT Int. Appl., 46pp.

CODEN: PIXXD2 DOCUMENT TYPE: Patent English

LANGUAGE: FAMILY ACC. NUM. COUNT: 1

	NO.		KIN						ICAT					ATE	
	128979													0070	
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	IS, IT,														
	532051				2009										
	89649				2009										
	109814				2008				008-					0081	
	012934				2008									0081	
	KN04414														
	0035804		A1		2010	0211								0090	
PRIORITY APE	LN. INFO	. :						GB 2	006-	6946		- 1	A 2	0060	406

W 20070405 The invention provides nucleic acid mols. encoding the circularly permuted human growth hormone GHCP07 and variants thereof,

wherein variants contain amino acid changes at the receptor binding sites and acts as growth hormone receptor antagonists. The

invention also provides the amino acid sequences of GHCP07, and antagonist GHCP07C, wherein GHCP07C contains a C-terminal region of human growth hormone (GH) linked to a N-terminal region of GH,

with a changes in amino acids at receptor binding sites, such as Glycine to Arginine at position 176. The invention further provides various fusion proteins comprised of: (a) at least two GHCP07C polypeptides linked in tandem; (b) extracellular binding domains of growth hormone receptor (GHR) linked to at least two GHCP07 polypeptides;

(c) GHCP07C polypeptides linked to a human prolactin modified polypeptide (such as G129R PRL); and/or (d) GHCP07C-human modified prolactin fusions containing an extracellular domain of receptors, such as cytokine, GH, prolactin receptors. The invention was based on the general knowledge that the G129R mutation in PRL and G120R mutation in GH disrupt the structural integrity of the two receptor sites, and results in proteins acting as receptor antagonists. Still further, the invention provides: (a) nucleic acid mols. encoding the disclosed fusion proteins and their use in construction of vectors for recombinant protein production; and (b) the amino acid sequences of said extracellilar domains found in human GHR and the modified human prolactin (G129R). Finally, the invention provides for the use of the disclosed antagonists, and/or their fusion proteins, and/or their nucleic acids in construction of a pharmaceutical compn which can be use to treat various conditions, such as gigantism, acromegaly, cancer,

diabetic retinopathy, diabetic nephropathy and/or other complications of

diabetes and/or GH excess. In the examples, the invention presented mol. genetics methods used to generate circularly permutated growth hormone antagonists GHCP07BHis and GHCP07C, and showed that both proteins had antagonistic activity.

OS.CITING REF COUNT: THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD 1 (1 CITINGS) REFERENCE COUNT: THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS 6

RECORD, ALL CITATIONS AVAILABLE IN THE RE FORMAT DUPLICATE 1

ANSWER 11 OF 16 MEDLINE on STN ACCESSION NUMBER: 2007527470 MEDLINE DOCUMENT NUMBER: PubMed ID: 17721547

A ligand-receptor fusion of growth TITLE:

hormone forms a dimer and is a potent long-acting agonist.

Wilkinson Ian R; Ferrandis Eric; Artymiuk Peter J AUTHOR: ; Teillot Marc; Soulard Chantal; Touvay Caroline;

Pradhananga Sarbendra L; Justice Sue; Wu Zida; Leung Kin C; Strasburger Christian J; Savers Jon R; Ross Richard J

CORPORATE SOURCE: School of Medicine and Biomedical Sciences, Royal Hallamshire Hospital, University of Sheffield, Sheffield

S10 2JF, UK. Nature medicine, (2007 Sep) Vol. 13, No. 9, pp. 1108-13. SOURCE:

Electronic Publication: 2007-08-26. Journal code: 9502015. ISSN: 1078-8956. L-ISSN: 1078-8956.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal: Article: (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English FILE SEGMENT: Priority Journals

ENTRY MONTH: 200803

AB

ENTRY DATE: Entered STN: 11 Sep 2007

Last Updated on STN: 13 Mar 2008

Entered Medline: 12 Mar 2008

AB Cytokine hormones have a short plasma half-life and require frequent administration. For example, growth hormone replacement involves daily injections. In common with other cytokines, the extracellular domain of the growth hormone receptor circulates as a binding protein, which naturally prolongs the biological half-life of growth hormone. Here we have studied the biological actions of a ligand-receptor fusion of growth hormone and the extracellular domain of its receptor. The genetically engineered ligand-receptor fusion protein was purified from mammalian cell culture. In rats, the ligand-receptor fusion had a 300-times reduced clearance as compared to native growth hormone, and a single injection promoted growth for 10 d, far exceeding the growth seen after administration of native growth hormone. The ligand-receptor fusion forms a reciprocal, head-to-tail dimer that provides a reservoir of inactive hormone similar to the natural reservoir of growth hormone and its

binding protein. In conclusion, a ligand-receptor fusion of cytokine to its extracellular receptor generates a potent, long-acting agonist with exceptionally slow absorption and elimination. This approach could be easily applied to other cytokines.

L6 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2006:104499 CAPLUS

DOCUMENT NUMBER: 144:219144

TITLE: Recombinant dimers of cytokine receptor-binding domains linked by inflexible helical linkers for

modulation of cytokine signaling

INVENTOR(S): Artymiuk, Peter; Pradhananga, Sarbendra;

Sayers, John; Ross, Richard

PATENT ASSIGNEE(S): Asterion Limited, UK SOURCE: PCT Int. Appl., 69 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 1

	TENT :				KIND DATE A2 20060202					APPL						ATE	
WO WO		0108 0108	91 91		A2 A9		2006	0427								0050	
WO		AE, CN, GE, LC, NG, SL,	AG, CO, GH, LK, NI, SM,	AL, CR, GM, LR, NO, SY,	AM, CU, HR, LS, NZ, TJ,	AT, CZ, HU, LT, OM, TM,	AU, DE, ID, LU, PG, TN, CY,	AZ, DK, IL, LV, PH, TR,	DM, IN, MA, PL, TT,	DZ, IS, MD, PT, TZ,	EC, JP, MG, RO, UA,	EE, KE, MK, RU, UG,	EG, KG, MN, SC, US,	ES, KM, MW, SD, UZ,	FI, KP, MX, SE, VC,	GB, KR, MZ, SG, VN,	GD, KZ, NA, SK, YU,
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CA	2005 2575 1771 R:	2661 441 467 AT,	84 BE,	BG,	A1 A1 A2 CH,	CY,	2006 2006	0202 0411 DE,	DK,	CA 2 EP 2 EE,	005- 005- ES,	2575 7615 FI,	441 93 FR,	GB,	21 GR,	0050 0050 HU,	718 718

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CN 101014616 A 20070808 CN 2005-80030121 20050718
JP 2008507292 T 20080313 JP 2007-523141 20050718
NZ 553224 A 20090531 NZ 2005-553224 20050718
RU 2391353 C2 20100610 RU 2007-106043 20050718
MX 2007001180 A 20070413 MX 2007-1180 20070126
RR 2007067678 A 20070628 RC 20077-073976 20070220
RR 891509 B1 20090406
IN 2007KN00631 A 20070706 IN 2007-KN631 20070221
RG 2009006221 A 2009014 KR 2008-729058 20081127
US 20090221477 A1 2009093 US 2009-658526 20090416
RITY APPLN. INFO::

GREAT GREAT AND ADDRESS OF BE 2004-16687 A 20040727
GB 2005-2839 A 20050211
W 2005-682826 W 20050718
KR 2007-703976 A3 20070220
GRMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
PRIORITY APPLN. INFO.:
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB We disclose therapeutic proteins comprising at least two domains capable
        of binding to a cytokine receptor, wherein the domains are connected by a
        peptide linker, wherein the linker optionally comprises a rigid alpha
        helical region. These proteins may act as agonists or antagonists of
        cytokine signaling. Thus, growth hormone
        receptor-binding growth hormone fragments were
        dimerized using a rigid or semi-rigid linker. The rigid linker comprised the motif A(EAAAK)nA, with n=1-5 preferred. These proteins were
        produced with transgenic E. coli. The growth hormone
        activity of these proteins was equal to or greater than growth
        hormone itself.
OS.CITING REF COUNT:
                                                   THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD
                                                   (3 CITINGS)
REFERENCE COUNT:
                                          3
                                                   THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
                                                    RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L6 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2004:878488 CAPLUS
DOCUMENT NUMBER:
                                        141:344597
TITLE:
                                        Chimeric proteins containing cytokine receptor binding
                                        domain and glycosylphosphatidylinositol anchor and
                                        their therapeutic uses
INVENTOR(S): Ross, Richard; Sayers, Jon; Artymiuk, Peter PATENT ASSIGNEE(S): Asterion Limited, UK
PCT Int. Appl., 40 pp.
                                         CODEN: PIXXD2
DOCUMENT TYPE:
                                        Patent
                                        English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
        PATENT NO. KIND DATE APPLICATION NO. DATE
        WO 2004090135 A2 20041021 WO 2004-GB1572
WO 2004090135 A3 20050428
                                                                                                                20040407
              2004090135

A3 20050428

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TD, TG
                         A2 20060118 EP 2004-726219
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PRIORITY APPLN. INFO .:
                                           GB 2003-8088
                                                              A 20030409
                                           GB 2003-24235
                                                               A 20031016
                                           WO 2004-GB1572
                                                               W 20040407
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
    The present invention relates to polypeptides which comprise a
    ligand-binding domain of a cytokine receptor fused with a signal sequence
    for the attachment of glycosylphosphatidylinositol (GPI) anchors.
    GPI-anchors are post-translational modifications to proteins that add
    glycosylphosphatidylinositol which enable these proteins to anchor to the
    extracellular side of cell membranes. 1B1-GP1 was constructed, in which
    GH was linked through its C-terminus to the extracellular domain of the GH
    receptor and then linked to the GPI signal sequence. 1C1-GPI was also
    constructed, in which a tandem of GH was linked through the second GH
    C-terminus to the GPI signal sequence. The invention provides vectors and
    CHO-K1 cells for expressing GHBP-GPI.
OS.CITING REF COUNT:
                        1
                              THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
                              (1 CITINGS)
REFERENCE COUNT:
                              THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
                              RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
    ANSWER 14 OF 16 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on
L6
ACCESSION NUMBER: 2004:225928 BIOSIS
DOCUMENT NUMBER:
                   PREV200400225966
TITLE:
                   Tandem fusions of growth hormone and
                   its G120R mutated antagonist retain biological activity and
                   demonstrate prolonged plasma half-life.
AUTHOR(S):
                   Pradhananga, S. L. [Reprint Author]; Wilkinson, I. [Reprint
                   Author]; Haylor, J. [Reprint Author]; Rezaee, S. [Reprint
                   Author]; Artymiuk, P.; Sayers, J.; Ross, R. J. M.
                   [Reprint Author]
CORPORATE SOURCE:
                   Department of Clinical Sciences, Sheffield University,
                   Sheffield, UK
SOURCE:
                   Growth Hormone & IGF Research, (April 2004) Vol. 14, No. 2,
                   pp. 116. print.
                   Meeting Info.: Second International GH-IGF Symposium.
                   Queensland, Australia. April 18-22, 2004.
                   ISSN: 1096-6374 (ISSN print).
DOCUMENT TYPE:
                   Conference; (Meeting)
                   Conference; Abstract; (Meeting Abstract)
                   English
LANGUAGE:
ENTRY DATE:
                   Entered STN: 21 Apr 2004
                   Last Updated on STN: 21 Apr 2004
L6 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:
                        2003:591215 CAPLUS
                        139:144956
```

DOCUMENT NUMBER: TITLE: Ligand binding domains of cytokine which are linked

via flexible polypeptide linker and uses in therapy INVENTOR(S): Ross, Richard; Artymiuk, Peter; Sayers, Jon

PATENT ASSIGNEE(S): Asterion Limited, UK SOURCE: PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent PATENT INFORMATION:

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	2003	0622	76		A2											2	0030	124
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							IN,											
							MD,											
							SD,											
							VN.						,	,	,	,	,	,
	RW:	GH,											UG.	ZM.	ZW.	AM.	AZ.	BY.
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							IE,											
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		AT,																
							RO,											,
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	2004																0040	
	2005																0050	
PRIORIT	Y APP	LN.	INFO	. :						GB	200	2-1	679			A 2	0020	125
															i		0030	
ASSIGNM	ENT H	ISTO	RY F	OR U	S PA	TENT	AVA	ILAB:										-

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention relates to the provision of oligomeric polypeptides (dimers,
trimers, etc) comprising the ligand binding domains of cytokines which are
linked via flexible polypeptide linker mols. The linker mols. optionally
comprise protease sensitive sites to modulate the release of biol. active

cytokines when administered to a human or animal subject. The invention also relates to chemical crosslinkers wherein the chemical crosslinkers serve

to

link the ligand binding domains. The chimeric cytokine can be used for treating acromegally, gigantism, GH deficiency, Turners syndrome, renal failure, osteoporosis, diabetes mellitus, cancer, obesity, insulin resistance, hyperlipidemia, hypertension, anemia, autoimmune and infectious disease, inflammatory disorders including rheumatoid arthritis. OS.CITING REF COUNT: 1 THERE ARE I CAPLUS RECORDS THAT CITE THIS RECORD

(1 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN ACCESSION NUMBER: 2001:924005 CAPLUS

DOCUMENT NUMBER: 136:49347

TITLE: Chimeric binding agent comprising cytokine, linker and

cytokine receptor and uses in modulating receptor

activity and therapy
INVENTOR(S): Ross, Richard: Artym

INVENTOR(S): Ross, Richard; Artymiuk, Peter; Sayers, Jon PATENT ASSIGNEE(S): Asterion Limited, UK

SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

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KIND DATE APPLICATION NO. DATE
     PATENT NO.
    WO 2001096565 A2 20011220 WO 2001-GB2645
WO 2001096565 A3 20020801
                                                                  20010618
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
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         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
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     CA 2447632
                         A1
                              20011220 CA 2001-2447632
20030312 EP 2001-940731
     EP 1290170
                         A2
                                                                  20010618
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                        T 20040205
A1 20040415
     JP 2004503243
                                           JP 2002-510682
                                                                   20010618
     US 20040071655
                                           US 2003-311473
                                                                   20030718
                        A1 20040415
B2 20081104
A1 20090226
     US 7446183
     US 20090054336
                                           US 2008-175582
                                                                   20080718
                                                              A 20000616
PRIORITY APPLN. INFO.:
                                            GB 2000-14765
                                                                A 20010310
                                            GB 2001-5969
                                            GB 2001-6487
                                                                A 20010316
                                            WO 2001-GB2645
                                            US 2003-311473
                                                                A1 20030718
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
   The invention provides a binding agent comprising a first part capable of
     binding a ligand binding domain of a receptor linked to a second part
     comprising a receptor binding domain wherein said binding agent modulates
     the activity of the receptor. The inventors link growth
     hormone (GH), through its C-terminal and a linker to the
    N-terminus of the SD100 domain of growth hormone
     receptor (GHR). By varying the length of the linker inventors define a
     mol. that has the flexibility to allow binding of GH through site 1 to
     full length receptor at the cell surface. The invention also relates to
     methods, vectors and host cells for production of said chimeric binding agent.
OS.CITING REF COUNT:
                        6
                              THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD
                               (6 CITINGS)
REFERENCE COUNT:
                              THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
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L2
             22 S L1 AND GROWTH (W) HORMONE
             19 DUP REM L2 (3 DUPLICATES REMOVED)
           363 S ARTYMIUK P?/AU
L4
L5
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L6
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L7
         11282 S ROSS R?/AU
1.8
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T.9
            28 S L8 AND LIGAND
1.10
            16 DUP REM L9 (12 DUPLICATES REMOVED)
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FILE 'STNGUIDE' ENTERED AT 15:01:53 ON 28 JUN 2010

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 15:09:50 ON 28 JUN 2010

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=> dis ibib abs 110 1-16

YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, CAPLUS' - CONTINUE? (Y) /N:y

L10 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:1048978 CAPLUS

DOCUMENT NUMBER: 151:307229

TITLE: Linker peptides including glycosylation sites for use

in fusion proteins

INVENTOR(S): Artymiuk, Peter; Ross, Richard; Sayers, Jon

Asterion Limited, UK PATENT ASSIGNEE(S):

PCT Int. Appl., 185pp. SOURCE: CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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		FI,	GB,	GD,	GE,	GH,	GM,	GT,	HN,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,
		KG,	KM,	KN,	KP,	KR,	KZ,	LA,	LC,	LK,	LR,	LS,	LT,	LU,	LY,	MA,	MD,
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PRIORITY	APP:	LN.	INFO	. :						GB 2	008-	2978		- 7	A 2	0800	219
										GB 2	008-	2107	6		A 2	0081	119
										GB 2	009-	539		- 1	A 2	0090	114

OTHER SOURCE(S): MARPAT 151:307229

Peptide linkers that contain a glycosylation site and that can be used in the manufacture of fusion proteins that interact with membranes, e.g. fusion proteins of proteins and their cognate receptors. Glycosylation site motif variants for use in linker peptides are described.

REFERENCE COUNT: THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS 6 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2009:115655 CAPLUS

150:161106 DOCUMENT NUMBER:

Growth hormone fusion proteins

Ross, Richard; Artymiuk, Peter; Sayers, Jon INVENTOR(S):

PATENT ASSIGNEE(S): Asterion Limited, UK SOURCE: PCT Int. Appl., 41pp.

CODEN: PIXXD2 DOCUMENT TYPE: Patent LANGUAGE: English

DOCUMENT TYPE: Patent

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KIND DATE APPLICATION NO. DATE
     PATENT NO.
     WO 2009013461 A1 20090129 WO 2008-GB2406 20080716
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              KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD,
             ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH,
              PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ,
              TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
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              TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
              AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
     AU 2008278907 A1 20090129 AU 2008-278907
CA 2693951 A1 20090129 CA 2008-2693951
EP 2170943 A1 20100407 EP 2008-775945
                                                                       20080716
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20080716
         R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI,
                          LI, LT, Lu, L., BA, MK, RS
A 20100428 KR 2010-702192
A 20100324 CN 2008-80021473 20091222
GB 2007-17985 A 20070720
GB 2007-17985 A 20070914
              SK, TR, AL, BA, MK, RS
     KR 2010043201 A 20100428
CN 101679504 A 20100324
PRIORITY APPLN. INFO.:
ΔR
     We disclose growth hormone fusion proteins that have
     increased in vivo stability and activity; nucleic acid mols. encoding said
     proteins and methods of treatment of growth hormone
     deficiency that use said proteins. This disclosure relates to the biol.
     actions of a ligand-receptor fusion (LR-fusion) of GH with its
     extracellular domain receptor. Such a genetically engineered LR-fusion
     protein was purified from mammalian cell culture. In rats the LR-fusion
     had a 300-times reduced clearance compared to native GH and single
     administration promoted growth for 10 days far superior to that seen with
     native GH. The reduced clearance is reproducible in a primate model. The
     LR-fusion forms a reciprocal, head-to-tail dimer that provides a reservoir
     of inactive hormone as occurs naturally with GH and its binding protein.
     A recombinant gene encoding human GH linked to the A & B domains of the
     GHR extracellular domain (exGHR1-238) via a flexible (Glv4Ser)4 linker,
     was generated (Fig. 1 c).
REFERENCE COUNT:
                          6
                                 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
                                 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L10 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2007:1303035 CAPLUS
DOCUMENT NUMBER:
                          147:535195
TITLE:
                          Fusion protein composed of circularly permuted
                          growth hormone antagonist GHCP07C,
                          extracellular domain of receptor, and human modified
                          prolactin, and its use in construction of
                          pharmaceutical compositions for treating disorders
INVENTOR(S):
                          Pradhananga, Sarbendra; Sayers, John; Ross,
PATENT ASSIGNEE(S): Richard; Artymiuk, Peter Asterion Limited, UK
SOURCE:
                          PCT Int. Appl., 46pp.
                          CODEN: PIXXD2
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LANGUAGE: Er
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

										APPLICATION NO.										
												2007-					0070	405		
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			KN,	KP,	KR,	KZ,	LA,	LC,	LK,	LR,	LS	, LT,	LU,	LY,	MA,	MD,	MG,	MK,		
			MN.	MW,	MX,	MY,	MZ,	NA,	NG,	NI,	NO	, NZ,	OM,	PG,	PH,	PL,	PT,	RO,		
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			ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW	, ML,	MR,	NE,	SN,	TD,	TG,	BW,		
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								ТJ,												
												2007-								
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	EP	2004	681			A1		2008	1224		EΡ	2007-	7323	29		2	0070	405		
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												2009-								
	CN	1013	8964	9		A		2009	0318		CN	2007-	8000	6944		2	0800	827		
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												2008-								
		2010				A1		2010	0211			2009-								
PRIO	RIT:	Y APP	LN.	INFO	.:							2006-								
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AB	The	a inv	ent i	on no	rovi	des i	nuc l	eic	acid	mo l	s.	encod	ina :	the	circ	nlar	lv n	ermut		

The invention provides nucleic acid mols. encoding the circularly permuted human growth hormone GHCP07 and variants thereof, wherein variants contain amino acid changes at the receptor binding sites and acts as growth hormone receptor antagonists. The invention also provides the amino acid sequences of GHCP07, and antagonist GHCP07C, wherein GHCP07C contains a C-terminal region of human growth hormone (GH) linked to a N-terminal region of GH, with a changes in amino acids at receptor binding sites, such as Glycine to Arginine at position 176. The invention further provides various fusion proteins comprised of: (a) at least two GHCP07C polypeptides linked in tandem; (b) extracellular binding domains of growth hormone receptor (GHR) linked to at least two GHCP07 polypeptides; (c) GHCP07C polypeptides linked to a human prolactin modified polypeptide (such as G129R PRL); and/or (d) GHCP07C-human modified prolactin fusions containing an extracellular domain of receptors, such as cytokine, GH, prolactin receptors. The invention was based on the general knowledge that the G129R mutation in PRL and G120R mutation in GH disrupt the structural integrity of the two receptor sites, and results in proteins acting as receptor antagonists. Still further, the invention provides: (a) nucleic acid mols. encoding the disclosed fusion proteins and their use in construction of vectors for recombinant protein production; and (b) the amino acid sequences of said extracellilar domains found in human GHR and the modified human prolactin (G129R). Finally, the invention provides for the use of the disclosed antagonists, and/or their fusion proteins, and/or their nucleic acids in construction of a pharmaceutical compn which can be use to treat various conditions, such as gigantism, acromegaly, cancer, diabetic retinopathy, diabetic nephropathy and/or other complications of diabetes and/or GH excess. In the examples, the invention presented mol. genetics methods used to generate circularly permutated growth

hormone antagonists GHCP07BHis and GHCP07C, and showed that both

proteins had antagonistic activity.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD

(1 CITINGS)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS

RECORD, ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 16 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2007527470 MEDLINE

DOCUMENT NUMBER: PubMed ID: 17721547

TITLE: A ligand-receptor fusion of growth

hormone forms a dimer and is a potent long-acting

agonist.

AUTHOR: Wilkinson Ian R; Ferrandis Eric; Artymiuk Peter J; Teillot

Marc; Soulard Chantal; Touvay Caroline; Pradhananga

Sarbendra L; Justice Sue; Wu Zida; Leung Kin C; Strasburger Christian J; Sayers Jon R; Ross Richard J

CORPORATE SOURCE: School of Medicine and Biomedical Sciences, Royal

Hallamshire Hospital, University of Sheffield, Sheffield

S10 2JF, UK.

Nature medicine, (2007 Sep) Vol. 13, No. 9, pp. 1108-13. SOURCE:

Electronic Publication: 2007-08-26.

Journal code: 9502015, ISSN: 1078-8956, L-ISSN: 1078-8956.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200803

ENTRY DATE: Entered STN: 11 Sep 2007

Last Updated on STN: 13 Mar 2008 Entered Medline: 12 Mar 2008

AB Cytokine hormones have a short plasma half-life and require frequent

administration. For example, growth hormone

replacement involves daily injections. In common with other cytokines,

the extracellular domain of the growth hormone

receptor circulates as a binding protein, which naturally prolongs the

biological half-life of growth hormone. Here we have studied the biological actions of a ligand-receptor fusion of

growth hormone and the extracellular domain of its

receptor. The genetically engineered ligand-receptor fusion

protein was purified from mammalian cell culture. In rats, the

ligand-receptor fusion had a 300-times reduced clearance as compared to native growth hormone, and a single

injection promoted growth for 10 d, far exceeding the growth seen after

administration of native growth hormone. The

ligand-receptor fusion forms a reciprocal, head-to-tail dimer that provides a reservoir of inactive hormone similar to the natural reservoir

of growth hormone and its binding protein. In

conclusion, a ligand-receptor fusion of cytokine to its extracellular receptor generates a potent, long-acting agonist with

exceptionally slow absorption and elimination. This approach could be easily applied to other cytokines.

L10 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2006:104499 CAPLUS

DOCUMENT NUMBER: 144:219144

TITLE: Recombinant dimers of cytokine receptor-binding domains linked by inflexible helical linkers for

modulation of cytokine signaling

INVENTOR(S): Artymiuk, Peter; Pradhananga, Sarbendra; Sayers, John; Ross, Richard
PATENT ASSIGNEE(S): Asterion Limit

PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2

Paten+

English

MAND DAME

DOCUMENT TYPE: LANGUAGE:

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

PA	TENT :	NO.			KIN	D	DATE				LICAT								
WO WO	2006 2006	0108: 0108:	91 91		A2 A9		2006	0427											
WO	2006	0108	91		A3		2006	0608											
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AU	2005	2661	84		A1		2006	0202		AU :	2005-	2661	84		2	0050	718		
CA	2575	441			A1		2006	0202		CA 2	2005-	2575	441		2	0050	718		
EP	1771	467			A2		2007	0411		EP :	2005-	7615	93		2	0050	718		
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											, PT,								
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KR	2007 2007 8915 2007	0676	78		A		2007	0628		KR 2	2007-	7039	76		2	0070	220		
KR	8915	09			В1		2009	0406											
IN	2007	KN00	631		A		2007	0706		IN 2	2007-1	KN63	1		2	0070			
	2009										2008-					0081			
	2009				A1		2009	0903			2009-					0090			
PRIORIT	Y APP	LN.	TNEO	. :							2004-								
											2004-					0040			

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB We disclose therapeutic proteins comprising at least two domains capable of binding to a cytokine receptor, wherein the domains are connected by a peptide linker, wherein the linker optionally comprises a rigid alpha helical region. These proteins may act as agonists or antagonists of cytokine signaling. Thus, growth hormone

receptor-binding growth hormone fragments were

dimerized using a rigid or semi-rigid linker. The rigid linker comprised the motif A(BAAAK)nA, with n = 1-5 preferred. These proteins were produced with transgenic E. coli. The growth hormone activity of these proteins was equal to or greater than growth

hormone itself.
OS.CITING REF COUNT: 3 THERE

3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

GB 2005-2839

WO 2005-GB2826

KR 2007-703976 A3 20070220

A 20050211

W 20050718

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 16 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 2006194908 MEDLINE DOCUMENT NUMBER: PubMed ID: 16464942

TITLE: A mutant signal transducer and activator of transcription

5b, associated with growth hormone

insensitivity and insulin-like growth factor-I deficiency, cannot function as a signal transducer or transcription

factor.

AUTHOR: Fang Peng; Kofoed Eric M; Little Brian M; Wang Xiangdong;

Ross Richard J M; Frank Stuart J; Hwa Vivian; Rosenfeld Ron G

CORPORATE SOURCE: Department of Pediatrics, NRC5, Oregon Health and Science

Department of Pediatrics, NRC5, Oregon Health and Science University, 3181 Southwest Sam Jackson Park Road, Portland,

OR 97239-3098, USA.

CONTRACT NUMBER: CA 58110 (United States NCI NIH HHS)
DK 46395 (United States NIDDK NIH HHS)

SOURCE: The Journal of clinical endocrinology and metabolism, (2006 Apr.) Vol. 91, No. 4, pp. 1526-34. Electronic Publication:

2006-02-07. Journal code: 0375362. ISSN: 0021-972X. L-ISSN: 0021-972X.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

(RESEARCH SUPPORT, N.I.H., EXTRAMURAL) (RESEARCH SUPPORT, NON-U.S. GOV'T)

(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200605

ENTRY DATE: Entered STN: 8 Apr 2006

Last Updated on STN: 2 May 2006

Entered Medline: 1 May 2006 CONTEXT: A natural missense mutation in the signal transducer and AB activator of transcription (STAT) 5b gene was recently identified in association with a female patient presenting with severe growth failure and immune dysfunction. The mutation results in an alanine to proline substitution at residue 630 (A630P) in the src-homology-2 domain, a region essential for docking of STATs to phospho-tyrosines on activated receptors, STAT dimerization, and stabilization of phospho-STAT-DNA interactions. OBJECTIVE: The purpose of this study was to explore the molecular mechanisms underlying the GH insensitivity and IGF-I deficiency caused by the A630P-mutated STAT5b. RESULTS: In reconstitution experiments using HEK293 cells, both GH and interferon-gamma were unable to activate mutant STAT5b (A630P), as demonstrated by lack of immunodetectable phospho-tyrosyl-STAT5b (A630P) and inability to drive luciferase reporter activity. However, the Src family of nonreceptor kinases [constitutively active v-src and epithelial growth factor-induced c-src] tyrosine-phosphorylated STAT5b(A630P). The v-src-induced phospho-STAT5b(A630P) translocated to the nucleus but, unlike wild-type Stat5b, was unable to bind DNA. CONCLUSIONS: The A630P mutation disrupts the src-homology-2 architecture such that: 1) mutant STAT5b most likely cannot dock to phospho-tyrosines on ligand-activated receptors; and 2) stable interactions with DNA are prevented. Because STAT5b (A630P) is an inefficient signal transducer and transcription factor, the detrimental impact on signaling pathways important for normal growth and immunity explains, in part, the complex clinical phenotype of GH insensitivity and immune dysfunction.

ACCESSION NUMBER: 2006076164 MEDITINE DOCUMENT NUMBER: PubMed ID: 16461551

TITLE: A 36 residues insertion in the dimerization domain of the

growth hormone receptor results in

defective trafficking rather than impaired signaling. Maamra M; Milward A; Esfahani H Zarkesh; Abbott L P; AUTHOR: Metherell L A; Savage M O; Clark A J L; Ross R J M

CORPORATE SOURCE: Division of Clinical Sciences (North), University of Sheffield, Clinical Sciences Centre, Northern General

Hospital, Sheffield S5 7AU, UK.

SOURCE: The Journal of endocrinology, (2006 Feb) Vol. 188, No. 2, pp. 251-61.

Journal code: 0375363. ISSN: 0022-0795. L-ISSN: 0022-0795. PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200604

ENTRY DATE: Entered STN: 8 Feb 2006

Last Updated on STN: 5 Apr 2006 Entered Medline: 4 Apr 2006

AB Growth hormone insensitivity syndrome (GHIS) has been

reported in a family homozygous for a point mutation in the GH receptor (GHR) that activates an intronic pseudoexon. The resultant GHR (GHR1-656) includes a 36 amino-acids insertion after residue 207, in the region known to be important for homodimerization of GHR. We have examined the functional consequences of such an insertion in mammalian cells transfected with the wild type (GHRwt) and mutated GHR (GHR1-656). Radioligand binding and flow cytometry analysis showed that GHR1-656 is poorly expressed at the cell surface compared with GHRwt. Total membrane binding and Western blot analysis showed no such difference in the level of total cellular GHR expressed for GHR1-656 vs GHRwt. Immunofluorescence showed GHR1-656 to have different cellular distribution to the wild type receptor (GHRwt), with the mutated GHR being mainly perinuclear and less vesicular than GHRwt. Western blot analysis showed GH-induced phosphorylation of Jak2 and Stat5 for both GHR1-656 and GHRwt, although reduced Stat5 activity was detected with GHR1-656, consistent with lower levels of expression of GHR1-656 than GHRwt at the cell surface. In conclusion, we report that GHIS, due to a 36 amino-acids insertion in the

defect rather than by a signalling defect of GHR. L10 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2005:34776 CAPLUS

DOCUMENT NUMBER: 142:127937

TITLE: Modified cytokine ligand polypeptides

preparation, screening, and uses thereof for treatment

extracellular domain of GHR, is likely to be explained by a trafficking

INVENTOR(S): Sayers, Jon; Artymuik, Peter; Ross, Richard

PATENT ASSIGNEE(S): Asterion Limited, UK SOURCE: PCT Int. Appl., 45 pp.

CODEN: PIXXD2 DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005003165	A2	20050113	WO 2004-GB2827	20040628
WO 2005003165	A.3	20050714		

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             SN, TD, TG
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                        A2 20060329 EP 2004-743175
B1 20100505
                                                                  20040628
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     JP 2008504001 T 20080214 JP 2006-518330
                        T
                                          AT 2004-743175
     AT 466880
                              20100515
                                                                  20040628
     US 20070264234
                       A1 20071115 US 2007-561831
                                                                  20070316
PRIORITY APPLN. INFO.:
                                           GB 2003-15182
                                                              A 20030628
                                           WO 2004-GB2827 W 20040628
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The disclosed invention describes modified cytokine ligand
     polypeptides comprising a modified amino acid sequence which is a
     modification of the native cytokine amino acid sequence of said
     ligand, wherein the native N terminal and C terminal amino acid
     residues of the native polypeptide are linked, directly or indirectly,
     together, characterized in that said ligand is provided with
     alternative N terminal and C terminal amino acid residues and further
     wherein at least one binding domain for said ligand's cognate
     binding partner or receptor complex is disrupted. The authors describe
    the first embodiment of the growth hormone circular
     permutation GH CP01, with the N terminus Ile121 and the C terminus Glu118.
     The "old" termini of GH were linked by a 6 amino acid linker, formed by
     joining the "old" termini -3 amino acids from the first helix at the N
     terminus and +3 residues for the last helix at the C terminus. E. coli
     cells were used as the expression system. Also described are alternative
     approaches to construct circular permutations of GH.
OS.CITING REF COUNT:
                              THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD
                               (2 CITINGS)
                              THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
REFERENCE COUNT:
                              RECORD, ALL CITATIONS AVAILABLE IN THE RE FORMAT
L10 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:
                     2004:878488 CAPLUS
DOCUMENT NUMBER:
                        141:344597
TITLE:
                        Chimeric proteins containing cytokine receptor binding
                        domain and glycosylphosphatidylinositol anchor and
                        their therapeutic uses
                      Ross, Richard; Sayers, Jon; Artymiuk, Peter
Asterion Limited, UK
PCT Int. Appl., 40 pp.
INVENTOR(S):
PATENT ASSIGNEE(S):
SOURCE:
                        CODEN: PIXXD2
DOCUMENT TYPE:
                        Patent
LANGUAGE:
                        English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
                KIND DATE APPLICATION NO. DATE
     PATENT NO.
    WO 2004090135 A2 20041021 WO 2004-GB1572 20040407
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WO 2004090135
                         A3
                                20050428
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             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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             SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
             TD, TG
    EP 1616010
                                20060118
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                                                                    20040407
                          A2
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     JP 2007527695
                          Т
                                20071004
                                           JP 2006-506114
                                                                    20040407
     US 20060205926
                                20060914
                                            US 2005-552388
                                                                    20051007
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     US 7625998
                          B2
                                20091201
PRIORITY APPLN. INFO.:
                                            GB 2003-8088
                                                                 A 20030409
                                            GB 2003-24235
                                                                 A 20031016
                                             WO 2004-GB1572
                                                                 W 20040407
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
    The present invention relates to polypeptides which comprise a
     ligand-binding domain of a cytokine receptor fused with a signal
     sequence for the attachment of glycosylphosphatidylinositol (GPI) anchors.
     GPI-anchors are post-translational modifications to proteins that add
     glycosylphosphatidylinositol which enable these proteins to anchor to the
     extracellular side of cell membranes. 1B1-GP1 was constructed, in which
     GH was linked through its C-terminus to the extracellular domain of the GH
     receptor and then linked to the GPI signal sequence. 1C1-GPI was also
     constructed, in which a tandem of GH was linked through the second GH
     C-terminus to the GPI signal sequence. The invention provides vectors and
     CHO-K1 cells for expressing GHBP-GPI.
OS.CITING REF COUNT:
                               THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
                         1
                               (1 CITINGS)
REFERENCE COUNT:
                               THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L10 ANSWER 10 OF 16
                         MEDLINE on STN
                                                         DUPLICATE 3
ACCESSION NUMBER:
                    2004448217
                                   MEDLINE
                    PubMed ID: 15356058
DOCUMENT NUMBER:
TITLE:
                    Pegvisomant, a growth hormone-specific
                    antagonist, undergoes cellular internalization.
                    Maamra M; Kopchick J J; Strasburger C J; Ross R J M
AUTHOR:
CORPORATE SOURCE:
                    Sheffield University, Clinical Sciences, Northern General
                    Hospital, Sheffield, United Kingdom.
                    The Journal of clinical endocrinology and metabolism, (2004
SOURCE:
                    Sep) Vol. 89, No. 9, pp. 4532-7.
                    Journal code: 0375362. ISSN: 0021-972X. L-ISSN: 0021-972X.
                    United States
PUB. COUNTRY:
DOCUMENT TYPE:
                    Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:
                    English
FILE SEGMENT:
                    Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:
                    200410
ENTRY DATE:
                    Entered STN: 10 Sep 2004
                    Last Updated on STN: 8 Oct 2004
                    Entered Medline: 7 Oct 2004
    GH binding to a receptor (GHR) dimer triggers signaling and
     internalization of the receptor/ligand complex. Pegvisomant is
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a specific GH antagonist developed for the treatment of acromegaly, and

AB

the basic molecule is GH with an amino acid substitution that blocks the conformational change necessary to generate functional GHR dimerization required for signal transduction. Pegvisomant has additional polyethylene glycol moieties to prolong its half-life in the circulation and improve clinical efficacy through reduced renal clearance. Pegvisomant has a long plasma half-life, and its mode of clearance has not been established. We have studied pegvisomant internalization and demonstrate that despite its size and prolonged plasma half-life, it is internalized by cells expressing the GHR. As pegvisomant does not activate intracellular signal transduction systems, our results support the concept that the conformational changes required for GHR signaling are not essential for the intracellular trafficking of the ligand and establish one potential contributing mechanism for pegvisomant clearance.

L10 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN ACCESSION NUMBER: 2003:591215 CAPLUS

DOCUMENT NUMBER: 139 - 144956

TITLE: Ligand binding domains of cytokine which are linked via flexible polypeptide linker and uses in

therapy

INVENTOR(S): Ross, Richard; Artymiuk, Peter; Savers, Jon PATENT ASSIGNEE(S): Asterion Limited, UK

PCT Int. Appl., 37 pp. SOURCE:

CODEN: PIXXD2 DOCUMENT TYPE: Patent.

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

PA'	TENT	NO.								APPL	ICAT	DATE					
					A2 20030731 A3 20031016 L, AM, AT, AU, AZ,				WO 2	003-	GB25	3		2	0030	124	
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	RW:	GH, KG, FI,	GM, KZ, FR,	KE, MD, GB,	LS, RU, GR,	MW, TJ, HU,	MZ, TM, IE,	SD, AT, IT,	SL, BE, LU,	SZ, BG, MC,	TZ, CH, NL,	CY, PT,	CZ, SE,	DE, SI,	DK, SK,	EE, TR,	ES,
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RU MX	2325 2004	400 0071	60		C2 20080527 A 20050331				RU 2 MX 2	004-	1219 7160	69		20030124 20030124 20040723 20040730			
US PRIORIT	2005 Y APP				A1		2005	0929		GB 2	005- 002- 003-	1679		1	A 2	0050 0020 0030	125

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

The invention relates to the provision of oligomeric polypeptides (dimers, trimers, etc) comprising the ligand binding domains of cytokines which are linked via flexible polypeptide linker mols. The linker mols. optionally comprise protease sensitive sites to modulate the release of biol. active cytokines when administered to a human or animal subject. The invention also relates to chemical crosslinkers wherein the chemical

crosslinkers serve to link the ligand binding domains. The chimeric cytokine can be used for treating acromegaly, gigantism, GH deficiency, Turners syndrome, renal failure, osteoporosis, diabetes mellitus, cancer, obesity, insulin resistance, hyperlipidemia,

hypertension, anemia, autoimmune and infectious disease, inflammatory disorders including rheumatoid arthritis.

OS.CITING REF COUNT: THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD 1

(1 CITINGS)

REFERENCE COUNT: THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:180984 CAPLUS

DOCUMENT NUMBER: 140:194483

TITLE: Chimeric proteins containing cytokine receptor binding domain and glycosylphosphatidylinositol-containing

signaling peptide and their therapeutic uses

INVENTOR(S): Ross, Richard

PATENT ASSIGNEE(S): Asterion Ltd., UK

SOURCE: PCT Int. Appl., 50 pp.

CODEN: PIXXD2 DOCUMENT TYPE: Patent

LANGUAGE: Enalish

FAMILY ACC. NUM. COUNT: 2 PATENT INFORMATION:

W0 2003034275	PA	TENT	NO.			KIND DATE					APPLICATION NO.									
Wi. AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MM, MX, MZ, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UG, UG, VC, VN, YU, ZA, ZM, ZW, GK, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, BF, BG, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG GB 2380735 A 20030416 GB 201-24620 20011013 CA 2494706 A1 20030424 JP 2003-356934 20021011 JP 3984492 B2 20091216 AU 2002334161 B2 20090329 AU 2002-344161 20021011 RU 2340628 C2 20081210 RD 2002-801405 20021011 RU 2340628 C2 20081210 RD 2002-801405 20021011 RI AT, BE, BG, CH, CY, CZ, DE, DK, EE, SF, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, SK, TR AT 442444 T 20099019 RF 2002-801405 20021011 RU 204001611 A3 20100128 HU 2004-1611 20021011	WO	2003	0342	75		A2		2003	0424											
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AT 442444 T 20090915 AT 2002-801405 20021011 HU 2004001611 A3 20100128 HU 2004-1611 20021011 KR 2010039911 A 20100416 KR 2010-707082 20021011																				
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US 20050059577 A1 20050317 US 2004-492403 20040413	US	US 20050059577						2005	0317		US	2004-	4924	03		2	0040	413		
US 7485713 B2 20090203	US		B2		2009	0203														
PRIORITY APPLN. INFO.: GB 2001-24620 A 20011013																				
GB 2002-904 A 20020116											GB	2002-	904			A 2	0020	116		
GB 2002-18889 A 20020814											GB	2002-	1888	9		A 2	0020	814		
GB 2002-18889 A 20020814 KR 2004-705419 A3 20021011											KR	2004-	7054	19		A3 2	0021	011		
WO 2002-GB4665 W 20021011											WO	2002-	GB46	65		W 2	0021	011		

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT AB The present invention relates to polypeptides which comprise a cytokine-binding domain of a cytokine receptor fused with a signal sequence for the attachment of glycosylphosphatidylinositol (GPI) anchors. The cytokine receptor variants lack a cytoplasmic domain and therefore do not have the capability to signal. The provision of a GPI-anchor domain means the variant inserts into membranes and acts as an effective inhibitor of GH signaling by competing for circulating cytokine and binding cytokine at the cell surface in a heterodimeric complex that consists of the chimeric truncated GPI anchored receptor, cytokine, and the native receptor. In addition, truncated GPI-anchored receptor generates a large amount of soluble receptor which will bind its ligand. In a preferred embodiment, the chimeric protein acts as an antagonist following local or transgenic expression through gene therapy. Thus, the cDNA extracellular domain of human growth hormone receptor (bases 98-834 of GenBank X06562) is ligated into a vector (pAc6-LP-MCS-GPI) containing the Dictyostelium actin 6 gene promoter, a Dictyostelium signal peptide coding region, multiple, cloning site, and the signal for a GPI anchor, and the construct is transfected into Dicytostelium cells. To demonstrate that growth hormone receptor-GPI can act as a transgenic therapy, the extracellular domain of the growth hormone receptor is cloned upstream of a human GPI signal sequence into a mammalian expression vector.

OS.CITING REF COUNT: THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD, ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2003:550165 CAPLUS

DOCUMENT NUMBER: 139:112729

TITLE: Chimeric growth hormone-

growth hormone receptor proteins and

therapeutic uses thereof INVENTOR(S): Ross, Richard; Savers, Jon; Artymuik, Peter

PATENT ASSIGNEE(S): Asterion Limited, UK

SOURCE: Brit. UK Pat. Appl., 46 pp. CODEN: BAXXDU

DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 2

PA:	TENT :	NO.			KIN	D	DATE			APPL	ICAT		DATE						
	2384				A		20030716 GB 2001-30052 20040204								2	0011	214		
	2384				B A		2004 2003			GR 2	กกจ_	2047	a a		2	0011	214		
	2389				В		2005			-	005				_	0011			
	2468				A1		2003					2468			20021206				
WO	2003	0707	65		A2		2003			WO 2	002-	GB55:		20021206					
WO	2003						2003												
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AU 2002366325 A1							2003	0909		AU 2	002-		20021206						

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AU 2002366325 B2 20080424 EP 1456385 A2 20040915 EP 2002-806858 20021206 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
 ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
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AB A chimeric polypeptide comprising at least one modified binding domain of growth hormone (GH) and a ligand binding

domain of growth hormone receptor (GHR) is claimed,

wherein the modification is the addition, deletion or substitution of at least one amino acid. Said binding domain may be site 1 of growth hormone, site 2 of growth hormone or both

sites of growth hormone. The binding domain of the

growth hormone receptor may be the extracellular domain

of GHR more preferably the C-terminal SD-100 domain. Nucleic acids encoding such polypeptides, expression vectors and cells expressing such vectors are also claimed. The use of such polypeptides in the preparation of pharmaceuticals and in the treatment of diseases including gigantism,

acromegaly, cancer and diabetic conditions is also claimed. Alternatively claimed is a chimeric polypeptide comprising more than two modified growth hormone binding domains.

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 5 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN ACCESSION NUMBER: 2003:300688 CAPLUS DOCUMENT NUMBER: 138:315840

TITLE: Preparation of GPI-anchored proteins with cytokine

receptor ligand binding domain and signal

sequence

INVENTOR(S): Ross, Richard

PATENT ASSIGNEE(S): Asterion Limited, UK

SOURCE: Brit. UK Pat. Appl., 41 pp. CODEN: BAXXDU

DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

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	GB	2380	735			A		2003	0416		GB	200	1-2	2462	0			200	110	013	
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PRIOR	PRIORITY APPLN. INFO.:										GB	200	1-3	2462	0		A	200	110	013	
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ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention relates to polypeptides which comprise a receptor binding domain of a cytokine and a domain which includes a signal sequence for the attachment of glycosylphosphhatidylinositol (GPI) anchors. The invention also relates to methods to manufacture the polypeptides, nucleic acids, mols. encoding the polypeptides and therapeutic compns. by comprising the polypeptides.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2010 ACS on STN ACCESSION NUMBER: 2001:924005 CAPLUS DOCUMENT NUMBER: 136:49347

TITLE: Chimeric binding agent comprising cytokine, linker and cytokine receptor and uses in modulating receptor

KIND DATE APPLICATION NO

DATE

activity and therapy

Ross, Richard; Artymiuk, Peter; Savers, Jon INVENTOR(S): PATENT ASSIGNEE(S): Asterion Limited, UK

SOURCE: PCT Int. Appl., 79 pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION: PATENT NO

TENT	NO.					DATE			APPL	ICAT	DATE					
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ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT The invention provides a binding agent comprising a first part capable of binding a ligand binding domain of a receptor linked to a second part comprising a receptor binding domain wherein said binding agent modulates the activity of the receptor. The inventors link growth hormone (GH), through its C-terminal and a linker to the N-terminus of the SD100 domain of growth hormone receptor (GHR). By varying the length of the linker inventors define a mol. that has the flexibility to allow binding of GH through site 1 to full length receptor at the cell surface. The invention also relates to methods, vectors and host cells for production of said chimeric binding agent.

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

REFERENCE COUNT: THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 16 OF 16 MEDLINE on STN DUPLICATE 4 ACCESSION NUMBER: 1999262630 MEDLINE DOCUMENT NUMBER: PubMed ID: 10329677

TITLE: Studies with a growth hormone antagonist and dual-fluorescent confocal microscopy

demonstrate that the full-length human growth hormone receptor, but not the truncated isoform, is very rapidly internalized independent of Jak2-Stat5

signaling.

AUTHOR: Maamra M; Finidori J; Von Laue S; Simon S; Justice S;

Webster J; Dower S; Ross R

CORPORATE SOURCE: Divisions of Clinical Sciences, Sheffield University,

Sheffield S5 7AU, United Kingdom.

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274, No. 21, pp. 14791-8.

Journal code: 2985121R. ISSN: 0021-9258. L-ISSN: 0021-9258.

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ENTRY MONTH: 199907 ENTRY DATE: Entered STN: 27 Jul 1999

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AB We have investigated trafficking of two negative regulators of growth hormone receptor (GHR) signaling: a human, truncated receptor, GHR1-279, and a GH antagonist, B2036.

Fluorescent-labeled growth hormone (GH) was rapidly internalized by the full-length GHR, with >80% of the hormone internalized within 5 min of exposure to GH. In contrast, <5% of labeled GH was internalized by cells expressing truncated GHR1-279. Using another truncated receptor, GHR1-317 fused to enhanced green fluorescent protein

(EGFP), we have exploited fluorescence energy transfer to monitor the

trafficking of ligand-receptor complexes. The data confirmed that internalization of this truncated receptor is very inefficient. It was possible to visualize the truncated GHR1-317-EGFP packaged in the endoplasmic reticulum, its rapid movement in membrane bound vesicles to the Golgi apparatus, and subsequent transport to the cell membrane. The GH antagonist, B2036, blocked Jak2-Stat5-mediated GHR signaling but was internalized with a similar time course to native GH. The results: 1) demonstrate the rapid internalization of GH when studied under physiological conditions; 2) confirm the hypothesis that internalization of cytoplasmic domain truncated human GHRs is very inefficient, which explains their dominant negative action; and 3) show that the antagonist action of B2036 is independent of receptor internalization.

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